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JPRS-ULS-90-020

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10 December 1990

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UDC 582.285.2:632.938

**Cytologic Investigation of Amine
Immunostimulant Effects on Fungus Puccinia
Graminis F. Sp. Tritici Development**

917C0020A Leningrad MIKOLOGIYA I

*FITOPATOLOGIYA in Russian Vol 24 No 3, May-Jun
90 (manuscript received 3 Jul 89) pp 216-220*

[Article by A. M. Yamaleyev, G. V. Serezhkina, and N. B. Troshina, Biochemistry and Cytochemistry Department, Bashkir Scientific Center, Ural Division, USSR Academy of Sciences, Ufa; Main Botanical Garden, USSR Academy of Sciences, Moscow]

[Abstract] The effects of plant immunostimulants bazuran [sic] (0.25 and 0.37 percent aqueous solutions) and bisol-2 (1.0 and 1.5 percent aqueous solutions) on the growth of uredospores of *Puccinia graminis* f. sp. *tritici* in vitro and on soft spring wheat Saratovskaya 29 plants were studied in both the ectophyte and endophyte stages of pathogen development. Exogenous treatment of the uredospores with bazuran and bisol-2 exhibited a dose-dependent effect, with bazuran increasing the number of uredospores with very branched germ tubes while bisol-2 increased the number of weakly branched, very long germ tubes. Both compounds affect the ectophyte and endophyte phases of development in all the application methods used (spraying plants, soaking seeds, and root system administration). The results demonstrated that the disruption of infection structure differentiation diminished the penetrating ability of the pathogen,

thus indicating that the pathologic process was suppressed by enhancing the natural resistance of the host plant. Of the two compounds, bazuran induced greater resistance in the plant to stem rust and better inhibited the endophytic development of the etiological agent. Figures 3; tables 2; references 7: 3 Russian, 4 Western.

UDC 633.11:632.938.12

**Fertility of First Generation Wheat x Wheatgrass
Hybrids**

907C0032B Moscow GENETIKA in Russian Vol 26 No 6, Jun 90 (manuscript received 10 Sep 89; in final form 27 Oct 89) pp 1129-1132

[Article by I. P. Titkov and V. M. Chekurov, Institute of Cytology and Genetics, Siberian Department, USSR Academy of Sciences, Novosibirsk]

[Abstract] F₁ generation wheat x wheatgrass (*Agropyron glaucum* and *A. elongatum*) hybrids were tested for fertility in pollination with pollen derived from a wide variety of wheat strains. Outcome analysis demonstrated that low fertility in the backcrossings was not due to the wheat, but attributable to the F₁ hybrids. Variable viability of the F₁ macrogametes was held responsible for the low fertility. Such heterogeneity in a single F₁ hybrid combination was due to the heterozygotic nature of the parental wheatgrass component. Tables 2; references 12 (Russian).

UDC 547.963.3

Location of C-Terminal Polyarginine Tract of HBcAg on Nucleocapsid Surface*907C0018x Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 312 No 4, Jun 90 (manuscript received 16 Nov 89) pp 993-996*

[Article by M. A. Bundule, V. V. Bychko, Yu. B. Saulitis, E. E. Liyepinsh, G. P. Borisova, I. A. Petrovskiy, V. V. Tsibinogin, P. P. Pumpen and E. Ya. Gren, corresp. member USSR Acad. Sci., Institute of Organic Synthesis, Latvian SSR Academy of Sciences, Riga]

[Abstract] ^{15}N -Arginine labeling and monoclonal antibodies were employed in assessing the disposition of C-terminal polyarginine fragment in the core nucleocapsid antigen (HBcAg) of hepatitis B virus. Analysis of the mobility of the fragment in NMR spectra and immunochemical localization with monoclonal antibodies specific for this tract demonstrated that the C-terminal polyarginine segment is located on the surface of the core nucleocapsid. Figures 2; references 13: 3 Russian, 10 Western.

UDC 577.152.314.04

Isolation and Properties of New Restriction Endonucleases from Haemophilus influenzae*907C0073A Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 16 No 7, Jul 90 (manuscript received 25 May 89; in final form 19 Dec 89) pp 889-897*

[Article by L. G. Lazaryavichyute, Z. P. Manyalene, A. M. Padegimene, L. Yu. Kyudulene, V. S. Lauchis, Yu. B. Bitinayte, I. M. Gruber*, V. M. Polyachenko*, V. V. Butkus and A. A. Yanulaytis, All-Union Scientific Research Institute of Applied Enzymology, Vilnius; *Central Scientific Research Institute of Vaccines and Sera imeni I. I. Mechnikov, USSR Academy of Medical Sciences, Moscow]

[Abstract] Screening studies on a variety of Haemophilus influenzae strains led to the identification of 11 restriction endonucleases, with delineation of the target sequences. On the basis of the substrate sequences, the newly-identified enzymes were identified as isoschizomers of known restriction endonucleases. In addition, specific cleavage sites (indicated by arrow) were determined for three of the restrictases: HinI I = (5')GR-CGYC; HinI II = (5')CATG-; and HibI III = (5')G-CGC. Figures 4; tables 3; references 11 (Western).

UDC 577.112.6.083.3

Synthetic Immunogenic Complexes of Surface Peptide of Foot-and-Mouth Virus*907C0073B Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 16 No 7, Jul 90 (manuscript received 23 Jan 89); 25 May 89) pp 904-915*

[Article by V. A. Rar, Ye. A. Makarov, V. V. Yurovskiy*, Ye. A. Meshcheryakova, T. M. Andronova and V. T.

Ivanov, Institute of Bioorganic Chemistry imeni M. M. Shemyakin (Moscow) and *Pushchino Branch of the Institute ((Moscow Oblast), USSR Academy of Sciences)]

[Abstract] A series of synthetic complexes of the C-terminal sequence (Ile-Val-Ala-Pro-Val-Lys-Gln-Thr-Leu; 205-213) of the surface VP₁ peptide of the foot-and-mouth disease virus, strain O₁K, were prepared for testing for immunogenicity. The immunogens included complexes synthesized by coupling the peptide to poly[D,L-Ala]_nLys (MW 130,000 D), maleic anhydride-vinylpyrrolidone copolymer (MW 50,000 D), N-acetyl-D-glucosaminyl(β 1-4)-N-acetylmuramoyl-alanyl-D-isoglutamine, bovine serum albumin, carbodiimide polymerized C-terminal sequence (MW 25,000 D). Intraperitoneal immunization of 15-20 g female Balb/c mice and ELISA assays demonstrated that the peptide-bovine serum albumin conjugate was the most immunogenic preparation. Tables 4; references 16: 4 Russian, 12 Western.

UDC 577.113.4.083.3

Identification of DNA Sequences by Antibodies Against trans-DDP-DNA Probes*907C0073C Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 16 No 7, Jul 90 (manuscript received 25 Dec 89) pp 991-992*

[Article by V. I. Kiseleva, M. F. Turchinskiy* and A. M. Poverenny, Scientific Research Institute of Medical Radiology, USSR Academy of Medical Sciences, Obninsk; *Institute of Bioorganic Chemistry imeni M. M. Shemyakin, USSR Academy of Sciences, Moscow]

[Abstract] Stable adducts between DNA and trans-diamminedichloroplatinum (trans-DDP) were synthesized to serve as probes in hybridization studies, with identification of the DNA sequences based on labeled antibodies directed against the adduct. Specific trials with plasmid pAT42 DNA as the target and a trans-DDP-DNA probe derived from the same plasmid after temperature denaturation of the DNA yielded a system with a sensitivity of 2 pg/mm² DNA on nitrocellulose filters. Figures 1; references 8: 1 Russian, 7 Western.

UDC 577.1:547.963.3

Cor Antigen of Hepatitis B Virus as Functionally Active Epitope Carrier: Exposure of PreS Sections on Capsids*917C0017A Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 312 No 3, May 90 (manuscript received 16 Nov 89) pp 751-754*

[Article by G. P. Borisova, I. G. Berzin, V. V. Tsibinogin, V. Ya. Loseva, P. M. Pushko, V. P. Ose, D. E. Dreylinya, P. P. Pumpen, and E. Ya. Gren, corresponding member, Organic Synthesis Institute, Latvian SSR Academy of

Sciences; Organic Synthesis Institute Experimental Factory, Latvian SSR Academy of Sciences; Microbiology Institute imeni A. Kirkhenshteyn, Latvian SSR Academy of Sciences]

[Abstract] The expression of the cor antigen gene in *Escherichia coli* results in the formation of a 25-27 nm in diameter capsid that is morphologically and functionally indistinguishable from native cor particles that form the nucleus of the hepatitis B virus. The cor antigen is currently being used in immunodiagnostics and in the construction of hepatitis vaccines. Interest is now directed at the potential for using the cor antigen as a foreign polypeptide sequence carrier and serves as the focus of this study.

For this purpose, an exposure vector was constructed to incorporate at pre-determined points of the gene natural or synthetic DNA copies of polypeptides that are of structural and functional interest with the observance of the following three basic conditions: 1. the inserted peptide retains its native conformation in chimeras; 2. it does not upset the capsid-forming properties of the latter; and 3. it is exposed on the peptide surface. Experimental proof of the potential for exhibiting oligopeptide sequences on the outer surface of the chimeric capsid with insertion of the respective DNA copy at the 144th amino acid gene (Pro_{144}), which plays an important role in forming the HBeAg antigen, was obtained employing plasmid pHbc1315 as the exposure vector. Results of this study demonstrated that the cor antigen may serve as a carrier of rather long foreign protein sequences. While the structure of the inserted section has little effect on the carrier's retention of capsid-forming properties, correct selection of the point at which the foreign sequences are inserted into the cor antigen gene are essential to retaining the capsid-forming properties of the carrier and localization of insertion on the capsid surface. The universality of this approach makes the construction of chimeras based on the cor antigen extremely promising in the development of new immunodiagnostic preparations and polyfunctional vaccines for preventing infectious diseases that differ greatly in their etiology. Figures 3; tables 1; references 15: 5 Russian, 10 Western.

UDC 577.112

Bradykinin Analogs and Other Vasoactive Peptides in Wasp *Polistes gallicus* Venom

907C0030A Tashkent KHIMIYA PRIRODNYKH
SOYEDINENIY in Russian No 3, May-Jun 90
(manuscript received 24 May 89) pp 389-393

[Article by I. F. Mukhamedov, V. M. Lvov and A. A. Akhunov, Institute of Bioorganic Chemistry imeni A. S. Sadykova, Uzbek SSR Academy of Sciences, Tashkent]

[Abstract] Chromatographic investigations on the venom of the wasp *Polistes gallicus* revealed 6 vasoactive peptides, 4 of which constituted congeners of bradykinin

with additional N- or C-terminal amino acids and internal substitutions. Two other peptides (I and V) represented unique sequences and did not cross-react with anti-bradykinin antibodies. In terms of myotropic activity (rat uterine horn) and hypotensive action (cats), 5 of the isolates were less potent than bradykinin. However, peptide I (Ile-Leu-Ala-Gly-Gly-Ile-Val-Lys-Lys-Leu) induced a 20 percent greater drop in BP with an i.v. dose of 28 $\mu\text{g/kg}$ than did bradykinin with an essentially equivalent [sic] dose of 10 $\mu\text{g/kg}$. Tables 3; references 11: 4 Russian, 7 Western.

UDC 577.213.7

Chemical Synthesis and Enzymatic Assembly of DNA Fragments Encoding Immunodominant HIV Epitopes

907C0030B Tashkent KHIMIYA PRIRODNYKH
SOYEDINENIY in Russian No 3, May-Jun 90
(manuscript received 4 Sep 89) pp 393-399

[Article by M. G. Isagulyants, S. V. Luchin and V. D. Smirnov, Institute of Virology imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences, Moscow; Institute of Molecular Biology imeni V. A. Engelhardt, USSR Academy of Sciences, Moscow]

[Abstract] The H-phosphonate method of oligonucleotide synthesis was combined with enzymatic assembly to generate DNA fragments encoding immunodominant epitopes of HIV-1. The encoding nucleotide sequences covered the following amino acid sequences: 598-609 and 737-748 of gp41, 99-115 and 105-115 of gag, and 940-951 of pol, as well as a series of analogous sequences. The target goal is the eventual engineering of *E. coli* for production of hybrid proteins expressing these epitopes. Figures 1; tables 1; references 22: 6 Russian, 16 Western.

UDC 547.94:577.152:612.815.1

Synthesis and Biological Activities of N-(β -Acyloxyethyl)Anabasine, Brucine, Strychnine and Cocaine Iodides

907C0030C Tashkent KHIMIYA PRIRODNYKH
SOYEDINENIY in Russian No 3, May-Jun 90
(manuscript received 6 Jul 89) pp 413-415

[Article by L. A. Srybnaya, Z. Tilyabayev, A. A. Sadykov and D. N. Dalimov, Institute of Bioorganic Chemistry imeni acad. A. S. Sadykov, Tashkent]

[Abstract] N-(β -acyloxyethyl)anabasine, brucine, strychnine and cocaine iodides were synthesized for screening against human erythrocyte acetylcholinesterase, horse equine butyrylcholinesterase and GABA-receptors. The results demonstrated that these agents inhibited both cholinesterases in a reversible manner. In addition, the cocaine, brucine and strychnine iodides bound to the benzodiazepine-binding segment of GABA-receptors, whereas the anabasine congener failed to do so. Accordingly, these

findings illustrate the ease with which the physiologic properties of alkaloids lend themselves to selective modification. References 6: 3 Russian, 3 Western.

UDC 541.69

Oligonucleotides Complementary to c-Ha-ras Gene m-RNA Which Suppress Proliferation of Human Cells in Culture

907C0846a Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 313, No 2, Jul 90 (manuscript received 20 Nov 86) pp 491-494

[Article by N. Debus, S. M. Gryaznov, and F. B. Berdichevskiy, Institute of Molecular Biology imeni V. A. Engelgardt, USSR Academy of Sciences, Moscow; Central Institute of Cancer Investigations, German Democratic Republic Academy of Sciences, Berlin]

[Abstract] The action of a synthetic oligodeoxynucleotide (ODN) complementary to c-Ha-ras 1 m-RNA on human embryonic fibroblast and bladder tumor cells in culture was studied. Effectiveness of ODN penetration was measured in two ways. In the first method biotinized desoxyuridinetriphosphate was used to label the 3'-OH terminus; histochemical staining was conducted with streptavidine conjugated to alkaline phosphatase. In the second method [³²P]-dATP and electrophoresis were used. In both cases the ODN was shown to appear in the cell within one hour. ODN synthesized with phosphothioester bonds persisted for 48 hours, longer than natural ODN. When the antisense ODN were added to the cells at around 10¹⁵ molecules per cell death of more than 90 percent of the cells was observed in 24 hours for the bladder tumor cells and in 48-72 hours for the fibroblasts. The level of c-Ha-ras expression is somewhat greater in the latter cells. Cell death was not seen when sense or universal sequence ODN were used. The data indicate that anti-ras may be used to cause reversion of malignant cells to a normal phenotype. This confirms previous results suggesting that ras plays a role in regulating cell proliferation and that in certain cell systems the ras protein is required for maintenance of viability. Figures 3; references 12: Western.

UDC 547.245:678.048

Biochemical Analysis of Stimulatory Action of Metalloatrans on Proliferation of Connective Tissue in Stomach Wall

907C0846d Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 313, No 2, Jul 90 (manuscript received 26 Jan 90) pp 501-504

[Article by M. M. Rasulov, I. G. Kuznetsov, L. I. Slutskiy, A. A. Belousov, and M. G. Voronkov, associate member, USSR Academy of Sciences, Irkutsk Institute of Organic

Chemistry, Siberian Department, USSR Academy of Sciences; All-Union Scientific Research and Design Institute of the Meat Industry, All-Union Academy of Agricultural Sciences imeni V. I. Lenin, Moscow]

[Abstract] The dynamics of the effect of organometallic triethanolamine esters (metalloatrans) on reparative processes were studied in damage to the connective tissue of the digestive tract. The compounds tested were 1-(chloromethyl)silatran (ChMS), methylethyl(silatran-1-ylmethyl)sulfone iodide (MESI), 1-(isopropoxy)-germatran (IPG) and the carbon analogue of silatran cresatsin. Effects were compared to those of 2,4-dioxo-6-methyl-1,2,3,4-tetrahydropyrimidine (metatsil, MU). White rats with acetate-induced ulcers were administered one of the compounds for ten days. All test preparations significantly accelerated epithelial repair and ulcer healing by the end of the observations (30 days), in comparison to untreated animals. Hexuronic acid levels were only slightly changed, with some normalization seen. Quantity of hexoseamine-containing glycoproteins decreased, as did hexose hypersecretion. All preparations decreased sialic acid levels. ChMS elicited stabilization of oxyproline levels at day 20. Peroxide oxidation of lipids was normalized. This suggests that antioxidant activity is involved in the mechanism of actions of the preparations. The membrane-stabilizing properties of the preparations are probably also involved. Figures 1; references 11: 7 Russian, 4 Western.

UDC 577.113.4

Solid Phase Synthesis of Biotinylated Oligodeoxyribonucleotides

907C0844a Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 313, No 1, Jul 90 (manuscript received 3 Jan 90) pp 214-216

[Article by V. P. Veyko, K. I. Ratmanova, A. S. Osipov, N. N. Veyko, A. V. Karpukhin, and V. G. Debabov, Associate Member, USSR Academy of Sciences; All-Union Scientific Research Institute of Genetics and Selection of Industrial Microorganisms; Institute of Medical Genetics, USSR Academy of Medical Sciences, Moscow]

[Abstract] A method for producing a nonradioactive labeled probe based on the oligodeoxyribonucleotide d(TAACCC)_n, and involving introduction of a biotin residue during synthesis via the H-phosphonate method, is reported. After the first condensation, the polymer was oxidized with 0.2 M iodine in absolute pyridine in the presence of 1,7-heptamethylenediamine. The dinucleotide obtained was treated with the N-oxy succinimide ester of N-biotinyl-6-aminocaproic acid. After this step-

the synthesis was continued until a 30-residue oligonucleotide was produced. Completeness of deblocking was confirmed by PAGE and homogeneity by reversed-phase HPLC. Hybridization of the product to a sample of total human genome, treated with HindIII restriction enzyme, and subsequent colorimetric determination of biotin

using streptavidine conjugate indicate that the sensitivity of the probe is as good as other nonradioactive probes previously reported, about 10^{-18} M oligonucleotide. The method developed permits biotin to be introduced at any desired internucleotide phosphate group. Figures 1; references 10: 3 Russian, 7 Western.

UDC 615.451.234:547.953].03

All-Union Program on Liposomes

917C0039A Moscow VESTNIK AKADEMII
MEDITSINSKIKH NAUK SSSR in Russian No 6, Jun
90 pp 3-7

[Article¹ by A. G. Chuchalin, academician of the USSR
Academy of Medical Sciences]

[Text]

Liposomes in Medicine

Liposomes are synthetic phospholipid vesicles, which were discovered 25 years ago. Since then, they have changed from an object of purely laboratory research, where they were used as models of biological membranes, into an object for broad medical and biological research of immediate practical interest at the present time. This is evidenced by the hundreds of scientific articles and patents, numerous monographs dealing with various aspects of biomedical use of liposomes, convocation of regular international meetings and conferences dedicated to the study and use of liposomes, primarily as drug vehicles in the body, publication abroad of a scientific periodical on problems of liposomes, establishment of a number of industrial companies producing liposomal drug and diagnostic agents and, finally, successful clinical trials and appearance on the pharmaceutical market of the first liposomal preparations for clinical use. The reason for this lies in the unique properties of liposomes as drug vehicles, which permit incorporation in their internal aqueous space of various water-soluble agents and into the lipid bilayer, of agents that are not water-soluble, and to specifically deliver them to the desired parts of the body, lower their toxicity and prolong their action in the body, protecting drugs against the aggressive physiological environment. In recent years, scientists and technologists have succeeded to a significant extent in solving problems related to obtaining liposomes, standardizing their size, producing sterile liposome preparations, storing them in suspension or lyophilized form, as well as providing for their stability in the body.

In addition to developing liposomal forms of known drugs and using liposomes themselves as drugs (for example, to control blood cholesterol levels or to treat certain lung diseases), the unique capacity of liposomes to deliver their contents into target cells is of great interest. This fact opens up essentially new possibilities for treatment of a broad spectrum of diseases related to functional impairment of cellular enzymes (liposomal and cytoplasmic), as well as to deliver foreign genetic material into cells.

It is of exceptional promise to use liposome as elements of diagnostic agents, where liposomes with enzyme molecules or a fluorescent marker contained in their internal aqueous phase are capable of enhancing a signal by many times due to release of enzyme or fluorogen into the external environment as a result of liposome breakdown under the effect of the target substance (direct or indirect, for example, complement-dependent lysis of liposomes).

In June 1988, within the framework of the Council for Biotechnology of the USSR Academy of Sciences, at a coordinating conference dealing with biomedical research on liposomes, there was discussion of the work being done in liposomology in the USSR, and the priority directions of research were defined. Representatives of virtually all teams of researchers involved in various aspects of biomedical use of liposomes in our country participated in the conference. The results of the conference were reported in a program that reflects the basic directions of development of liposomology in the USSR in 1989-1995. The program has the goal of organizing better defined, specially targeted and interrelated research in this field. The program sections deal with both basic and applied research. Basic research will be concerned with investigation of physicochemical properties of liposomes, structural and functional distinctions of liposomal membranes, and interaction between liposomes and cells. There will be studies of stability and distribution of liposomes in the body, and other aspects will also be covered.

In this program, attention is focused mainly on research that could result in development of medical and veterinary agents for treatment and prevention of disease. It includes work on recovery of naturally occurring and synthetic material to produce liposome agents, investigations on production of diagnostic agents for *in vivo* and *in vitro* use, agents for treatment of oncological diseases, as well as for treatment and prevention of infectious diseases. Due attention will be given to development of agents to activate the immune system, liposome preparations for pulmonology, liposomal forms of antibiotics, as well as radioprotective agents. Development of research on guided delivery of drugs into cells should be considered an important section of the program. Much attention will be also given to problems of technology, production of liposomes and liposomal agents on an industrial scale, their sterilization, standardization and storage. The solution to problems set forth in the program is of substantial relevance to theoretical and clinical medicine.

Footnote

1. Data are published in Numbers 6 and 8, 1990 [of this periodical].

**All-Union Program: "Liposomes and Their Use in Biology and Medicine"
(scientific and scientific-practical part of program)**

Codes, names of assignments and stages of program	Ministries and agencies responsible for solving problems, executor organizations (head, co-executors)	Deadlines (year, quarter)		Expected results of research (scientific and practical)	Expected form of adoption (level of adoption, target dates)	Expected impact (medico-social and economic)
		start	finish			
Investigation of physicochemical properties of liposomes (structural and functional distinctions of liposomal membrane), interaction of liposomes with cells, their stability and distribution in the body	USSR AMS, USSR MH, USSR AS, MSU, Uk AS, Uzbek AS*	1989	1995	Obtaining new data on properties differing in structure and phase, mechanisms of their interaction with normal and transformed cells, as well as immunocompetent cells	Inventions, efficiency proposals, methodological recommendations, information letters, monographs; dissertations (candidatorial and doctoral) defended, articles published, papers delivered at conferences and symposiums, etc.	Methods will be developed to register processes occurring during interaction of liposomes with various cells, and recommendations will be offered on optimum composition of liposomes for different purposes; methods will be developed for selective biodistribution of liposomes and recovery of pH-sensitive, polymerized and other uncommon liposomes
Recovery of naturally occurring and synthetic material for production of liposomal agents	Minmedmikrobioprom	1989	1995	Development of methods for synthesis of lipids with simple and complex bonds, as well as labeled with various markers; development of lipids capable of polymerization (developer: MITKhT)	Inventions, methodological recommendations, efficiency proposals, papers at conferences and symposiums, publication of articles	There will be expansion of the catalogue of lipids produced in the USSR, reduction of expenses in hard currency to acquire them from developed countries; it will become possible to sell domestic products abroad
Development of diagnostic agents for <i>in vivo</i> and <i>in vitro</i> use				Development of methods of isolating lipids from natural raw material: development and introduction of industrial methods of recovering lecithin from squid gonads (developers: KhE, DVGU, MITKhT, DKhTI, Atlant, NiRO, KIBP, Gidrorbybrom PO "Litrybprom"). Development and recovery of lecithin from animal brains (developer: Sanitas)	Same	
Development of diagnostic agents for <i>in vivo</i> and <i>in vitro</i> use	USSR MH	1989	1995	Completion of Clinical trials and submittal of VFS for the product Lipotrast used to contrast renal and hepatic vessels (developer: VNIRRI)	"	Introduction of agents into health care practice; improvement of quality of diagnosing diseases of the liver and kidneys, possibility of their earlier detection
				Development of liposomal signal enhancers for diagnostic sets (developer: VKNTs)		Elaboration of new immunological diagnostic methods

All-Union Program: "Liposomes and Their Use in Biology and Medicine"
(scientific and scientific-practical part of program) (Continued)

Codes, names of assignments and stages of program	Ministries and agencies responsible for solving problems, executor organizations (head, co-executors)	Deadlines (year, quarter)		Expected results of research (scientific and practical)	Expected form of adoption (level of adoption, target dates)	Expected impact (medico-social and economic)
		start	finish			
				Development of liposomes with a "transfer factor" for demonstration of deficient cell immunity to ubiquitous pathogens (developer: VNII of Vaccines and Sera imeni Mechnikov)		Development of a new method of assessing immunity to infections, which leads to optimization of treatment programs and prevention of infectious diseases
				Development of methods of using liposomal forms of alkyl esters of glycerin for cultural detection of tuberculosis (developers: IEM imeni Gamaleya USSR AMS, MIT-KhT)		Development of a new method of diagnosing tuberculosis
Development of methods for delivery of immunoactive factors incorporated in liposomes to microcompartments of the immune system (in particular to macrophage cytoplasm)	USSR AMS, USSR MH, Uzbek AS	1989	1995	Development of methods of delivering immunoactive factors incorporated in liposomes to microcompartments of the immune system, in particular to macrophage cytoplasm (Institute of Human Morphology USSR AMS, NII of Biomedical Technology, VKNTs)	"	Development of agents that enhance immune system resistance to diseases (including oncological ones); treatment and prevention of oncological and infectious diseases
				Development of immunostimulators based on liposomal forms of alkyl glycerol- and glycolipids (MITKhT, IEM imeni Gamaleya USSR AMS)		Development of agents that enhance immune system resistance to diseases (including oncological ones); treatment and prevention of oncological and infectious diseases
				Development of a method of obtaining liposomes with increased affinity for macrophages (VKNTs, Institute of Biochemistry Uzbek AS)		Development of agents that enhance immune system resistance to diseases (including oncological ones); treatment and prevention of oncological and infectious diseases
Development of liposomal agents for pulmonology	Uk AS, Minmedmikrobioprom	1989	1995	Development of liposomal forms of agents for treatment of hypoxic states (institutes of physiology and biochemistry of Uk AS)		

**All-Union Program: "Liposomes and Their Use in Biology and Medicine"
(scientific and scientific-practical part of program) (Continued)**

Codes, names of assignments and stages of program	Ministries and agencies responsible for solving problems, executor organizations (head, co-executors)	Deadlines (year, quarter)		Expected results of research (scientific and practical)	Expected form of adoption (level of adoption, target dates)	Expected impact (medico-social and economic)
		start	finish			
Development of liposomal agents for pulmonology	USSR AS, Minmed-mikrobioprom	1989	1995	Development of liposome suspensions and aerosols for treatment of surfactant deficiency in the lungs (Institute of Biochemistry Uk AS, Sanitas, VKNTs, Institute of Cardiology Kirghiz MH)	"	Development and clinical trial of Lipin and aerosols for normalization of surfactant composition of lungs
Development of liposome vaccines	USSR MH, USSR AMS, Uzbek AS, Biotechnology NPO, USSR Agroprom	1989	1995	Production and trial of meningococcus vaccine (NII of Vaccines and Sera imeni Mechnikov, VKNTs, Institute of Biochemistry Uzbek AS)	"	Preclinical and clinical trials of meningococcus vaccine
				Production and Trial of liposomal influenza vaccine (NII of Viral Products, VKNTs USSR AMS, Institute of Biochemistry Uzbek AS)		Preclinical and clinical trials of influenza vaccine
				Development and trial of liposomal rabies vaccine (Biotechnology NPO, Institute of Virology imeni Ivanovskiy USSR AMS)		Preclinical and clinical trials of rabies vaccine
Liposomes in oncology	USSR MH	1989	1995	Development of Liposomal forms of antineoplastic agents with low toxicity (NII of Biomedical Technology)	"	Preclinical and clinical trials of antineoplastic agents
				Development of liposomal forms of antimetastatic agents (Institute of Biochemistry Uzbek AS)		Preclinical trials of antimetastatic agents
				Development of targeted delivery in liposomes of agents against tumors (NII of Oncology imeni Gertsen, VKNTs USSR AMS)		Preclinical trials of targeted delivery of antineoplastic agents in liposomes
Treatment of infectious diseases	USSR MH	1989	1995	Development of liposomal forms of antibacterials for treatment of tuberculosis (NII of tuberculosis)	"	Preclinical and clinical trials of antibacterial antituberculosis agents
				Development of liposomal agents for herpes treatment (Institute of Virology imeni Ivanovskiy USSR AMS)		Preclinical and clinical trials of antiherpes agents

**All-Union Program: "Liposomes and Their Use in Biology and Medicine"
(scientific and scientific-practical part of program) (Continued)**

Codes, names of assignments and stages of program	Ministries and agencies responsible for solving problems, executor organizations (head, co-executors)	Deadlines (year, quarter)		Expected results of research (scientific and practical)	Expected form of adoption (level of adoption, target dates)	Expected impact (medico-social and economic)
		start	finish			
				Development of liposomal agents for treatment of brucellosis (Stavropol Plague-Control NII of the Caucasus and Trans-Caucasus, Biotechnology NPO)		Preclinical trials of antibrucellosis agents
Treatment of infectious diseases		1989	1995	Development of liposomal preparations of interferon for treatment of herpes (Biotechnology NPO, IEM imeni Gamaleya USSR AMS, VKNTs USSR AMS)	"	Preclinical trials of liposomal interferon
General problems of obtaining liposomal forms of biologically active compounds	USSR MH, Minmed-mikrobioprom	1989	1995	Development of liposomal forms of drugs based on chelating agents for treatment of occupational heavy metal poisoning (NII of Biomedical Technology USSR MH, NII of Biophysics USSR MH)	"	Preclinical and clinical trials of developed liposome preparations
				Development of liposomal preparations for treatment of acute massive necrosis of the liver of diverse etiology (NII of Biomedical Technology USSR MH)		Preclinical and clinical trials of developed liposome preparations
				Development of liposomal antibacterial agents (Kharkov Pharmaceutical Institute)		Preclinical and clinical trials of antibacterials
				Development of liposomal insulin preparations (Sanitas)		Preclinical and clinical trials of liposomal insulin
Liposomal antibiotics	USSR AMS, Uk MH	1989	1995	Development of methods of producing liposomal tetracycline, rifampicin and gentamicin (Kharkov Medical Institute)	"	Trial of new agents on experimental infections, preclinical trials
Targeted delivery of drugs into cells	USSR AMS, USSR MH	1989	1995	Development of pH-sensitive immunoliposomes capable of intracytoplasmic delivery of agents carried in liposomes (VKNTs USSR AMS)	"	Testing new agents on animals, preclinical trials

**All-Union Program: "Liposomes and Their Use in Biology and Medicine"
(scientific and scientific-practical part of program) (Continued)**

Codes, names of assignments and stages of program	Ministries and agencies responsible for solving problems, executor organizations (head, co-executors)	Deadlines (year, quarter)		Expected results of research (scientific and practical)	Expected form of adoption (level of adoption, target dates)	Expected impact (medico-social and economic)
		start	finish			
				Development of protein-modified liposomes capable of selective interaction with target cells (VKNTs USSR AMS, NII of Oncology imeni Gertsen)		Preclinical trials of new antineoplastic agents
				Development of liposomes modified by monoclonal antibodies against glycoprotein P15E of tumors (Institute of Human Morphology USSR AMS)		Preclinical trials of selective antineoplastic agents
Liposomal forms of selective drugs; basic research to expedite introduction of liposomal forms of drugs to health care practice	VNIRRI, VKNTs, USSR AMS, Biotechnology NPO, KhE, Sanitas, VNII of Biotechnology, USSR MH	1989	1995	Development of temporary pharmacopeia listings of pharmacological agents for the most promising phospholipids of the KhE (standard lecithin, phosphoinositid, cardiolipin, etc.) and cholesterol from the Leningrad Meat-Packing Plant, and toxicological monitoring of these agents	Pharmacopeia listings, methodological letters	Simpler and more convenient use of these agents for introduction to clinical practice
				Development of methodological recommendations in the section of "Methodological Guidelines" of the Pharmaceutical Committee of the USSR MS on preclinical and clinical investigation of new liposomal forms of drugs.		Elaboration of unified methodological recommendations for introduction to clinical practice of liposomal agents
				Technological and pharmacological research, preparation and submittal to Pharmaceutical Committee of the USSR MH of a complete list of documents on "hollow" liposomes from lecithin and cholesterol		Elaboration of unified methodological recommendations for introduction of liposomal agents
Technology for industrial recovery, sterilization and storage of liposomes	USSR MH, Minmedmikrobioprom, USSR AMS			Development of unified technology for industrial production, methods for sterilization by radiation and means of extending storage time		Introduction to practice of documentation on production, sterilization and storage of liposomes

**All-Union Program: "Liposomes and Their Use in Biology and Medicine"
(scientific and scientific-practical part of program) (Continued)**

Codes, names of assignments and stages of program	Ministries and agencies responsible for solving problems, executor organizations (head, co-executors)	Deadlines (year, quarter)		Expected results of research (scientific and practical)	Expected form of adoption (level of adoption, target dates)	Expected impact (medico-social and economic)
		start	finish			

Note: The institutes responsible for implementation of the research portion of the program are: VKNTs USSR AMS, Institute of Bioorganic Chemistry USSR AS, MGU, Institute of Biochemistry Uk AS, Institute of Biochemistry Uzbek AS.

*Expansions [in alphabetical order]: Agroprom—agroindustrial associations; AMS—Academy of Medical Sciences; AS—Academy of Sciences; DKhTI—Dnepropetrovsk Technological Chemistry Institute imeni F. E. Dzerzhinskiy; DVGU—Far East State University; IEM—Institute of Epidemiology and Microbiology; KhE—Kharkov Enterprise for Viral and Bacterial Agents; KIBP—expansion unknown; Gidroybprom—Hydraulic Engineering and Fisheries; Litrybprom—Lithuanian Fisheries; MH—Ministry of Health; Minmedmikrobioprom—Ministry of the Medical Microbiological Industry; MITKhT—Moscow Institute of Fine Chemical Technology imeni M. V. Lomonosov; MSU—Moscow State University; NIRO—Scientific Research Institute of Sea Fisheries and Oceanography; NPO—scientific-production association; PO—production association; Uk—Ukrainian; VFS—expansion unknown; VKNTs—All-Union Cardiological Research Center; VNII—All-Union Scientific Research Institute; VNIRRI—expansion unknown.

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UDC 591.15:575.113

Microinjection of Human Growth Hormone Releasing Factor in Zygotes and Embryos of Swine

917C0050A Moscow DOKLADY VSESOYUZNOY ORDENA LENINA I ORDENA TRUDOVOGO KRASNOGO ZNAMENI AKADEMII SELSKOKHOZYAYSTVENNYKH NAUK IMENI V. I. LENINA in Russian No 7, Jul 90 pp 46-51

[Article by L. Ye. Andreyeva, N. V. Khaydarova, L. I. Solodukhina, A. K. Vasil'ev, Yu. M. Kuznetsov, and K. G. Gazaryan, Institute of Molecular Genetics, USSR Academy of Sciences; Northern Caucasus Scientific Research Institute of Animal Husbandry]

[Abstract] Experiments were performed on microinjection of the human growth factor releasing hormone into swine zygotes and embryos. 75 pigs were produced in the experiments, 6 of which were transgenic. One transgenic animal reproduced, and some of the progeny inherited the transgene. The purpose of the studies was to determine the possibility of using the human growth hormone releasing factor gene to obtain transgenic swine. The product of this gene is known to regulate the expression of other genes, causing accelerated growth in ontogenesis, with both males and females remaining fertile. Two transgenic animals are still alive and well. References 9: 4 Russian, 5 Western.

UDC

579.861.2:579.222:577.112.7:[579.222:615.919:579.25:577.212.3:575.222.75

Construction of Recombinant Genes Producing Proteins Bearing Fragments of Protein A (Staphylococcus aureus) and Exotoxin A (Pseudomonas aeruginosa)

907C0078C Moscow MOLEKULYARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA in Russian No 7, Jul 90 (manuscript received 28 Dec 89) pp 27-32

[Article by A. G. Zdanovskiy, M. V. Zdanovskaya and N. K. Yankovskiy, All-Union Scientific Research Institute of Genetics and Selection of Industrial Microorganisms, Moscow]

[Abstract] Technical details are presented on the construction of recombinant genes encoding chimeric proteins bearing fragments of protein A (PA; Staphylococcus aureus) and exotoxin A (ETA; Pseudomonas aeruginosa). The final goal was production of immunotoxins combining the immunoglobulin-binding domain of PA and an ETA fragment lacking the Ia domain (which is responsible for ETA binding to eukaryotic cell, but still capable of promoting ADP-ribosylation of EF2.) Final steps involved recombination between a plasmid bearing the immunoglobulin-binding fragment of PA and one bearing the ETA toxoid, yielding a plasmid designated pAPA4. E. coli cells bearing pAPA4 were found to accumulate a 78 kD chimeric protein binding to rabbit immunoglobulins and possessing ADP-ribosyltransferase activity. Expression of the recombinant gene on pAPA4 was under the control of the lac operon. Figures 4; tables 1; references 22: 3 Russian, 19 Western.

UDC 633.71

Optimal Regeneration of Tobacco Protoplasts Treated with Exogenous DNA

907C0087A Moscow in Russian No 4, Jul-Aug 90 (manuscript received 14 Jul 88) pp 13-15

[Article by P. G. Kovalenko, A. P. Galkin and F. P. Galushko, Institute of Bioorganic Chemistry, Ukrainian SSR Academy of Sciences, Kiev]

[Abstract] Trials were conducted on optimizing regeneration of tobacco (Nicotiana tabacum SR-1) protoplasts

treated with thymic DNA to define parameters yielding a high rate plant regeneration from single colonies in 50-60 days. Experience with mesophilic protoplasts treated with thymic DNA, employing conventional methodology, demonstrated that acceleration of cell division was favored by plating of the protoplasts on 0.08 percent agarose within several days of DNA treatment. Agarose was found to be less toxic than agar and division was much greater than in liquid Kao-MMichayluk nutrient medium. Subsequent steps involved plating on 2 percent agarose, which favored initiation of morphogenetic transformation in procallus disks. An additional factor that elevated plating efficiency was represented by cold-synchronization (4°C for 10 days) of mitosis. Figures 3; tables 1; references 17: 2 Russian, 15 Western.

UDC 628.3

Bacterial Degradation of Ampholytic Surfactants

907C0087B Moscow in Russian No 4, Jul-Aug 90
(manuscript received 21 Mar 88) pp 31-33

[Article by L. A. Taranov, L. F. Ovcharov and M. N. Rotmistrov, Institute of Colloid Chemistry and Water Chemistry imeni A. V. Dumanskiy, Ukrainian SSR Academy of Sciences, Kiev]

[Abstract] Screening trials with *Pseudomonas* and *Citrobacter* spp. led to identification of species efficient in biodegradation of selected ampholytic surfactants. Specifically, batch cultures of *Ps. desmolytica* C37 utilized 500 mg/liter of cyclimide as the sole source of carbon and nitrogen over a 48 h period. In addition, immobilized mixed cultures of *Ps. putida* TO (47-51 percent), *Pseudomonas* sp. 1 (29-32 percent), and *C. freundii* (16 percent) were found capable of utilizing 500 mg/liter of amidobetaine, cyclimide, and alkylamino (bis) propionate. *Ps. stutzeri* AT was found to degrade amidobetaine at a rate of 200 mg/liter under batch conditions, a figure increasing to 400 mg/liter on immobilization. Finally, DNA analysis revealed that in the case of *Ps. putida* TO and *Ps. stutzeri* AT biodegradation of the surfactants was mediated by plasmids. Tables 3; references 19: 12 Russian, 7 Western.

UDC 628.4

Methane Generation from Municipal Solid Organic Wastes

907C0087C Moscow in Russian No 4, Jul-Aug 90
(manuscript received 23 Mar 89) pp 49-53

[Article by Ye. S. Pantskhava and Ye. V. Davidenko, Institute of Biochemistry imeni A. N. Bakh, USSR Academy of Sciences, Moscow]

[Abstract] Various testing modalities were employed for assessing methane production from solid organic wastes generated in cities, employing active sludge adapted to 33 and 53°C. The waste products consisted of 39.9

percent paper wastes, 46.0 percent food wastes, 1.8 percent textiles, 0.8 percent wood products and 11.5 percent particles < 16 mm in size, with a moisture content of 20 percent. Factor analysis of the various fermentation technologies demonstrated that in a recirculating mode the methane content of the biogas could be raised to 60-65 percent. Over a 28 day period the methane yield rose to 337 ml/g of the dry organic waste. Figures 1; tables 3; references 5 (Russian).

UDC 663.14.033

Algorithms and Software Support for Automatic Control of Fermentation in Biomass Production

907C0087D Moscow in Russian No 4, Jul-Aug 90
(manuscript received 25 Nov 87) pp 69-72

[Article by V. D. Kozlov, I. M. Chirkov, V. S. Bendeberi and V. V. Arakelyan, 'Promavtomatika' Scientific Industrial Association, Gorznyi]

[Abstract] Descriptive information is provided for algorithms and software employed in automated control of fermentation by methane oxidizing bacteria at the Svetlyy Yar biotechnology plant. Comparison of the production and productivity parameters attained by manual and computer-based (TP-10 G system) controls showed that automation resulted in a 13 percent increase in productivity of vitamin-protein concentrate. The cost effectiveness of the automation was clearly reflected in diminished utilization of nutrient medium, natural gas, and oxygen for equivalent biomass production. Figures 6; tables 1; references 6 (Russian).

UDC 615.281.2.073

Immunochemical Studies on Recombinant Human B-Interferon (RHBI)

907C0087E Moscow in Russian No 4, Jul-Aug 90
(manuscript received 24 Mar 89) pp 79-83

[Article by A. S. Ryzhavskaia, L. S. Izotova, S. V. Kostov, M. A. Skvortsova, V. E. Sterkin, S. V. Mashko and A. Ya. Strongin, All-Union Scientific Research Institute of Genetics and Selection of Industrial Microorganisms, Moscow]

[Abstract] Immunoenzyme assay (IEA) and radioimmunoassay methodologies were developed for native human β -interferon and RHBI for use in screening studies on genetically engineered producing bacteria. Both assays were rapid (5.5 h), exhibited high sensitivity (0.25-0.5 ng/L or 50-100 IU/ml) and reproducibility, and yielded results comparable with the activity of RHBI against vesicular stomatitis virus in human diploid fibro

blast culture. Screening studies showed that *Methylobacillus flagellatum*, *Serratia marcescens*, *Pseudomonas putida* and *Escherichia coli* produced from 10^5 to 10^9 IU/ml of RHBI. The highest producer was identified as *E. coli* K802 lon (pPR β -18) in which thermoregulated expression of the RHBI gene was under the control of P_r promoter. The maximum yield with this strain was

20-25 mg/L ($4-5 \times 10^9$ IU/L) of RHBI 1.5-2.0 h after thermoinduction. Immunoblotting, IEA, and electrophoretic studies demonstrated that at concentrations approaching 0.1 mg/L (2×10^7 IU/ml) RHBI remains soluble, but at higher concentrations becomes insoluble, adsorbs to cell detritus, and complicates recovery. Figures 5; tables 2; references 11: 1 Russian, 10 Western.

UDC 598/.9.15

Population-Demographic Structure of Columba Livia in Colonies in Kiev and the Area of the Chernobyl Nuclear Power Plant

917C0049A Moscow ZOOLOGICHESKIY ZHURNAL
in Russian Vol 69 No 7, Jul 90 pp 117-121

[Article by N. Yu. Obukhov, Department of Biology,
Moscow State University]

[Abstract] The population of the pigeon columba livia varies as a result of complex interactions among individuals. In long-established colonies the frequencies of individuals of various colors is quite constant, and can be changed only by severe changes in the environment. Such changes did occur in the vicinity of the Chernobyl Nuclear Power Plant in 1986. This article presents an analysis of the population-demographic structure of colonies of pigeons (Columba Livia Gm.) inhabiting the area where the human population was evacuated: the relationship of young and mature birds, the sexual composition, frequency of phenotypes, physiological and morphologic status of individuals and nature of reproduction. All of these reactions can indicate the degree of influence of the radioactive contamination or processes occurring in the populations in a territory abandoned by man. In the year after the accident there was a significant decrease in the number of gray and mixed color birds with an increase in the percentage of aberrant forms, possibly because the domestic pigeons abandoned the area with the humans. The percentage of young birds in Chernobyl was also unusually small, less than half the number of mature birds. There were no signs of high embryonal or postembryonal mortality, but clearly fewer birds were involved in reproduction, possibly a result of hormonal disorders. No

signs of disease were observed. In a later survey the percentage of birds in Chernobyl with ornithosis was lower than in Kiev, probably due to the lower population of young birds. References 2: Russian.

UDC 550.42:546.027

Comparative Analysis of Radionuclide Migration in Pond Silt Near Chernobyl Nuclear Power Plant

907C0031A Kiev DOKLADY AKADEMII NAUK
UKRAINSKOY SSR: SERIYA
B—GEOLOGICHESKIYE, KHIMICHESKIYE I
BIOLOGICHESKIYE NAUKI in Russian No 8, Aug 90
(manuscript received 12 Jan 90) pp 12-16

[Article by E. V. Sobotovich, corresp. member, UkrSSR Acad. Sci., Yu. A. Olkhovik, T. I. Koromyslichenko and G. A. Sokolik, Institute of Geochemistry and Mineral Physics, Ukrainian SSR Academy of Sciences]

[Abstract] Monitoring studies were conducted on the migration of radionuclides discharged in the Chernobyl Nuclear Power Plant accident in the silt and other sedimentary components of a cooling pond and the Krasnenskiy Reservoir, both within 30 km from the plant. The results demonstrated that some 5-7 percent of the Cs-137 and Sr-90 in the hot particulate matter became water soluble, while ca. 15 percent was leached as a result of ion-exchange mechanisms. In addition, approximately 14 percent of Ce-144 leached from the fuel particles entered the organic phase of the sediments, largely the humic and fulvic acid components. The rate constant for solubilization of the fuel particles was calculated at $K = 3 \times 10^{-7} \text{ sec}^{-1}$ based on Sr-90 and Cs-137 data, and can be expected to vary between 10^{-9} sec^{-1} and 10^{-8} sec^{-1} . Figures 2; tables 1.

Measures Planned for Preventing Diphtheria Epidemic in Moscow

917C0007B Moscow SOVETSKAYA ROSSIYA in Russian 30 Aug 90 Second Edition p 4

[Article by N. Barabash: "The Disease Caught Us Unawares"]

[Text] Nine deaths, 178 patients—such are today's unfortunate consequences of Moscow's diphtheria epidemic, reported earlier in the press.

Last week the Moscow City Soviet of People's Deputies conducted a meeting of the extraordinary epidemic control commission, during which special measures to fight the disease were worked out.

But is the epidemic really an extraordinary occurrence? Alas, the return of the dangerous infection was preprogrammed in many ways. The disease simply capitalized on the fact that we weren't ready for it. Actually the situation seemed to be favorable: While prior to 1956 over 20,000 persons suffered diphtheria annually in Moscow, and around a thousand died due to it, after introduction of mass vaccinations the number of patients dropped dramatically, and in 1975 for example, not a single diagnosis of "diphtheria" was made in the capital.

The doctors relaxed, and they continually lengthened the list of contraindications to immunization of children, such that even a simple diathesis became an obstacle here. Parents began refusing to have their children immunized: The mass media persuaded them that the risk from vaccination is greater than from the disease. And although workers of the USSR and RSFSR ministries of health assert that our vaccines correspond to international norms, and are widely used abroad, while the number of severe complications following immunizations is minimal—one case in a million, the number of unvaccinated children became increasingly larger with every year. Now only 49 percent of children are vaccinated in time in Moscow, even though in Europe this figure is 80 percent.

It is no surprise that the number of diphtheria cases began to grow in 1980. Forty-six people had it in the capital in 1988, and 94 had it in 1989. And so we have the outbreak of an epidemic. In the opinion of specialists, other factors such as the decline in natural immunity of adults, population migrations and accumulation of refugees also had an effect here. As of today, infection foci have been registered at the Kazan Train Station, in Children's Home No 5 in Kirovskiy Rayon, in Children's Boarding School No 15 in Kuntsevskiy Rayon, and in the Korall beer bar.

Tomorrow they may appear in other places, since the number of sick people, and consequently the number of people in contact with them, is growing. "How do we prevent the epidemic's spread in Moscow?"—this was with this question that we turned to N. N. Filatov, director of the epidemiological department of the Moscow City

Epidemiological Station on the eve of a meeting of the extraordinary epidemic control commission.

"Although I would say that the situation is critical, we are prepared to ward off an epidemic in Moscow," he said. "For this, we will subject the population to expanded immunization. The risk group has already been determined—workers in transportation, communication, the militia and the services, builders, and doctors. These categories of the population will be immunized on first priority by associates of the epidemiological teams being created in each rayon. Vaccinations will also be given to any persons desiring them: Immunization stations will be operating in one polyclinic of each rayon beginning next week. And of course, we will turn special attention to timely vaccination of children."

Diphtheria Outbreak in Moscow

917C0007A Moscow VECHERNYAYA MOSKVA in Russian 29 Aug 90 p 1

[Interview with epidemiological physician Galina Kostyuchenko by M. Pavlova, GUZM Health Center: "Who Is Being Urged to Get Immunized? We Are!"]

[Text] We have forgotten that diphtheria can kill, and even that this disease exists. But recent data say that a new outbreak of diphtheria has occurred. This year 174 Muskovites fell ill, and nine persons died, three of them children. The number of patients grows with every year. In 1988 there were 46 cases, in 1989 there were 94, and this year there have been almost twice more in less than 8 months. Why?

This question is answered by Galina Kostyuchenko, a physician and epidemiologist for the city public health station, who has dealt with the problems of diphtheria for over 30 years:

[Kostyuchenko] The fact is that refusals to receive AKDS [anti-whooping cough, diphtheria, tetanus] immunizations protecting children against whooping cough, diphtheria and tetanus have grown more frequent. Parents explain their refusal by the danger of infection of the children with AIDS virus, by the absence of disposable syringes, and by the presence of toxins in the vaccine, even though our vaccine corresponds to international standards. I have immunized my own children, and I advise parents not to refuse immunizations, since the risk is too high.

[Pavlova] Does immunization provide a guarantee against illness?

[Kostyuchenko] Against illness, no, but against a lethal and a serious outcome, yes. The fact is that there are two kinds of immunity—antibacterial and antitoxic. Antibacterial immunity against diphtheria does not exist, while antitoxic immunity is provided by immunizations. The disease proceeds mildly, and without consequences. We need to remember that diphtheria can also strike adults, even if the individual had it in childhood. The

antitoxic properties of immunization last for approximately 10 years, such that it must be repeated.

[Pavlova] How is diphtheria transmitted?

[Kostyuchenko] Dropwise through air, and by contact with objects and with dishware. Large accumulations of people are dangerous, especially in public transportation and in other crowded and stuffy places. We need to keep buildings, subway cars, streetcars, buses and trolleys clean.

[Pavlova] What are the signs of disease?

[Kostyuchenko] They are similar to angina. Temperature rises abruptly, the tonsils become inflamed, and edema develops on the 4th-5th days. Angina patients need to be subjected to bacterial testing at home, so that they might be hospitalized in time. In the presence of angina, the physician is obligated to keep the patient's condition under observation for 3 days, and to make visits automatically.

Let me repeat once again that both children and adults need preventive immunizations.

616.98:579.834.114]-07(47+57)

First Results and Objectives of Investigation of Lyme Disease in the USSR

917C0039B Moscow VESTNIK AKADEMII
MEDITSINSKIKH NAUK SSSR in Russian No 6, Jun
90 (manuscript received 7 Apr 89) pp 52-57

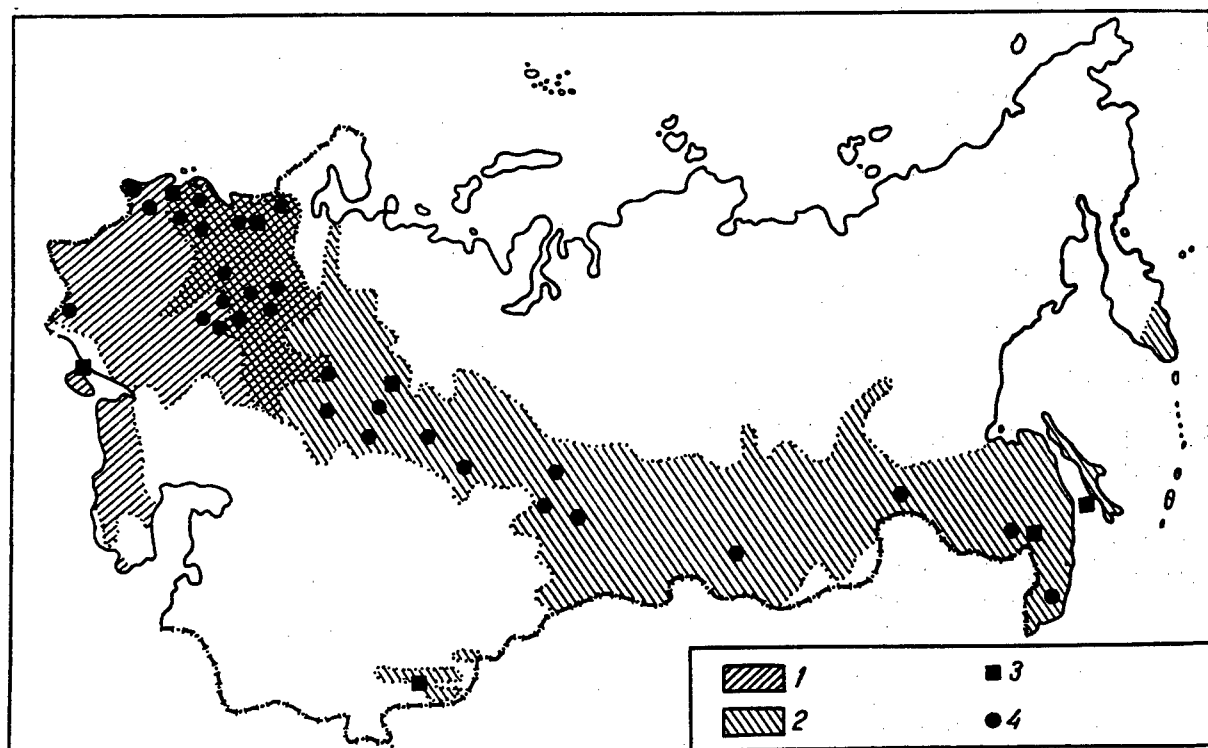
[Article¹ by E. I. Korenberg, V. N. Kryuchevnikov, and Yu. V. Kovalevskiy, Scientific Research Institute of Epidemiology and Microbiology imeni N. F. Gamaleya, USSR Academy of Medical Sciences, Moscow]

[Text] Lyme disease, which has been long known to dermatologists, neurologists and rheumatologists for its diverse clinical manifestations and under numerous names [14], is a relatively new nosological form to science. Its spirochetal etiology was discovered in the United States in 1981 [38], and in 1984 it was established that the pathogen is a new species of the genus *Borrelia*. It was named *Borrelia burgdorferi* [41]. After this intense investigation of different aspects of the problem of Lyme disease was launched. It is now apparent that this is a classical endemic, obligate transmissible borreliosis, the pathogen of which is extremely widespread, mainly in the forest belt of the temperate climate zone and, consequently, in many countries situated there [13, 45], and that the main vectors are ticks, predominantly of the genus *Ixodes* [14]. Being a systemic chronic or recurrent disease capable of striking the central nervous and cardiovascular systems, as well as the musculoskeletal system, Lyme disease presents a great danger to human health and can lead to lengthy inability to work and, in the case of severe late manifestations, to disability.

Clinical and epidemiological studies that preceded discovery of the pathogen of Lyme disease, as well as the way in which its etiology was identified in the United States and some European countries have been well-described in several special articles [14, 30, 32, 37, 47]. However, information pertaining to our country which was published in the foreign press [40] is fragmentary and rather biased. In this regard, it is opportune to stress that typical delayed dermatological manifestations of Lyme disease, known as chronic atrophic acrodermatitis were described by several Russian dermatologists under different names (independent atrophy of the skin; atrophica cutis maculata, idiopathic acquired cutaneous atrophy) as far back as the late 19th century and early 20th century [21, 22, 24-26]. These articles were published before the one in which A. Afzelius [31] offered the first description of early cutaneous manifestation of the disease, chronic migrating erythema (*erythema chronicum migrans*). In the 1950's, the special dissertation of N. D. Lisovskaya [18] dealt with the symptomatology of chronic atrophic acrodermatitis. At the same time, neurologists called attention to a disease that occurred after an *Ixodes* tick bite, which was associated with extensive ("tick-caused annular") erythema, various neurological disturbances without clear-cut serological confirmation of their relation to tick-borne encephalitis [19, 23, 28]. The opinion was expounded that this constituted the so-called erythematous form of tick-borne encephalitis. However, some researchers made a clear distinction between this disease and tick-borne encephalitis, and long before the discovery of *B. burgdorferi* they correctly assumed its etiological independence [17, 29]. In some oblasts, for example, Leningrad Oblast, the diagnosis of "tick-borne annular erythema" had been made for many years on hospitalized patients. Subsequent, more detailed clinical descriptions [1, 2, 27] and retrospective serological studies warrant the belief to assume with a large degree of certainty that at least a considerable number of such cases were Lyme borreliosis [3, 8, 13].

Special studies of the etiology, seroepidemiology and endemicity of this disease were begun in our country at the laboratory of infection vectors of the Scientific Research Institute of Epidemiology and Microbiology imeni N. F. Gamaleya, USSR Academy of Medical Sciences, in 1984, with preparation of the first survey in our scientific literature [14]. Subsequently, these investigations were carried out jointly by several scientific and clinical institutions with the support of the RSFSR Ministry of Health. First of all, it was necessary to prove that this infection existed in the USSR and to gain an idea about its possible distribution and significance in infectious pathology.

The American microbiologist, A. Barbour, who sent type strains of the pathogen, offered us inestimable support at the first stage of this work. They were cultured on BSK-2 medium [34], which enabled us to obtain corpuscular antigen for the indirect immunofluorescence reaction (nRIF) and to set up tests of serum from recovering patients using a method developed in our laboratory for borreliosis [15]. Thus, in 1985 Lyme disease was serologically confirmed for the first time in the USSR by



Distribution of Lyme borreliosis in the USSR

Key: 1—range of *I. ricinus* tick; 2—range of *I. persulcatus* tick; 3—site of isolation of pathogen; 4—site of serologically confirmed cases of disease in man.

testing blood serum of patients from the clinic of the Institute of Poliomyelitis and Viral Encephalitis of the USSR Academy of Medical Sciences [9, 39], and its presence in several regions was then indicated [13]. To date, cases of this borreliosis have been serologically identified in Estonian, Latvian, Moldavian SSR and RSFSR, and within the latter in 25 major administrative regions (Kalinigrad, Leningrad, Pskov, Yaroslavl, Kostroma, Vologda, Kalinin, Moscow, Vladimir, Ryazan, Tula, Sverdlovsk, Chelyabinsk, Tyumen, Omsk, Kemerovo, Novosibirsk, Tomsk, Irkutsk and Amur oblasts, Karelian, Udmurt and Bashkir ASSR, Khabarovsk and Maritime krays). There is no doubt that this list will grow appreciably in the immediate future, since material for testing has not yet been received from many regions. However, it already confirms entirely our opinion [13, 42] of the wide distribution of Lyme disease in the forest belt of the Soviet Union, from the Baltic region to the Far East. This means that the longest and perhaps largest area of the worldwide nosological range of Lyme disease is within the confines of our country (see Figure). The geography of borreliosis is closely related to the ranges of *I. ricinus* and *I. persulcatus* ticks, which are its main vectors in the USSR, and for this reason it is very similar to the distribution of tick-borne encephalitis. As with this infection, there are "ricinus" endemic sites of Lyme disease in western USSR and "persulcatus" sites more to the east, whereas in a considerable part

of East Europe, where both *I. ricinus* and *I. persulcatus* are encountered in forest stands [7], there are sites with both tick species [8, 10, 13].

These views have been confirmed, not only by the results of searching for borrelia in *I. ricinus* and *I. persulcatus* ticks under a microscope, but isolation from them of the first Soviet strains of *B. burgdorferi* from endemic sites in Khabarovsk Kray, Leningrad and Sverdlovsk oblasts, Lithuanian SSR, South Sakhalin, Kirghizia and Crimea. While our studies of *I. ricinus* merely confirmed foreign data [32, 33], *I. persulcatus* is a newly discovered one and, considering its enormous range [6], it is the most important vector of Lyme disease [10, 16].

Serological identification revealed that most of the strains we isolated were closer to European than American ones with regard to type of reaction with monoclonal antibodies. One of the strains (Ip-90) isolated from *I. persulcatus* from Khabarovsk Kray, is rather original in this respect [16]. Fractionation in polyacrylamide gel, which was carried out by Dr. A. Barbour, revealed a 20-22 kD protein wanting in most of the strains of *B. burgdorferi* studied in the world. Further investigation will, no doubt, determine the degree of taxonomic independence of this strain. But, generally speaking, on the basis of data already published, it can be considered that *B. burgdorferi* is characterized by rather considerable antigenic and serological polymorphism,

caused by the vast range of this pathogen and diversity of biocenotic structure of parasite systems in which it circulates. Perhaps expressly this explains some of the differences already detected in both early [20] and later [40] clinical manifestations of the disease in our country and the United States. In our opinion, we cannot rule out the possibility that the name of Lyme disease covers an entire group of etiologically independent forms of borreliosis. The first attempt has already been made to isolate several *B. burgdorferi* serogroups on the basis of nature of interaction with monoclonal antibodies and composition of antigenic protein fractions [35, 48]. According to our experimental data [16], at least two of them exist in the USSR.

At the same time, one cannot fail to take into consideration the fact that *B. recurrentis*, as well as several pathogens found in many countries but taxonomically poorly studied [11, 36], which are transmitted by Argas ticks, for example, Central Asian tick-borne borreliosis (ticks, for example, *B. burgdorferi* serogroups on the basis of nature of interaction with monoclonal antibodies and composition of antigenic protein fractions [35, 48]. According to our experimental data [16], at least two of them exist in the USSR.

From the theoretically point of view, it is extremely interesting to explore the problem of borrelia evolution, their ecological links to different groups of arthropods and paleogenesis of borreliosis. In order to carry out these tasks, as well as many purely practical ones, it is imperative, first of all, to have a wide assortment of strains. For this reason, a collection already containing about 30 *B. burgdorferi* cultures, including the American standard and a few Swedish reference strains, as well as our strains isolated in the USSR and Czechoslovakia, was started in the laboratory of vectors of infections at the Scientific Research Institute of Epidemiology and Microbiology imeni N. F. Gamaleya, USSR Academy of Medical Sciences. In addition, it includes strains of *B. persica* and *B. recurrentis*. We believe it is quite important to further expand this collection of borrelia, which is the only one in the USSR for the time being.

With respect to development of suitable approaches to serological detection of Lyme borreliosis, first of all the question arose of suitability for this purpose of the modification of the nRIF which we used [15]. A special study was carried out at the National Bacteriological Laboratory of Sweden of the sensitivity and specificity of this reaction in a parallel experiment with appropriate diagnostic agents produced by the USSR and Sweden. For this purpose, serum from recovering patients were used, which we had first tested with Soviet diagnostic serum and antigen. The results of the experiment were of findings identical and indicated good reproducibility of findings made in the USSR. In another experiment, carried out with the staff of the same laboratory (*B. Hederstedt*, *E. Jshizaki*), more than 140 serum samples

from recovering patients in Leningrad Oblast, which we had first tested using the nRIF, were checked with the immune enzyme test (ELISA [enzyme-linked immunosorbent assay]) with soluble antigen from the Swedish ACA-1 reference strain. This experiment yielded good results, indicative of the expediency of using the immune enzyme method provided appropriate equipment and sufficient amounts of bacterial material to prepare soluble antigen are available. However, as applied to the matter of mass-scale laboratory testing for Lyme disease, it is important that no appreciable advantages were found in the ELISA test, as compared to nRIF, with respect to specificity.

Serological confirmation of Lyme disease long after onset does not usually present any difficulty. Early detection of borreliosis is of enormous practical importance, since it responds readily to antibiotic therapy at that time, whereas without specific treatment it could change to the serious, systemic, chronic form. The opinion that an erythematous cutaneous lesion spreading from a tick bite is a clinical marker to diagnose the disease [40] is only partially valid. The presence of extensive and typical chronic erythema does indeed indicate borrelia infection in most cases, but its absence in victims of a tick bite does not provide grounds to rule out Lyme disease. Thus, according to our data, in 1987, about 20 percent of the serologically confirmed new cases in Leningrad Oblast were not associated with erythema. There are no other distinct clinical, differential-diagnostic signs of onset of Lyme disease. In such a situation, serological testing is particularly important. We analyzed the results of nRIF testing of about 230 serum samples obtained in 1987 from borreliosis patients in Leningrad Oblast at different times following the infective tick bite. We found that even in patients who were given antibiotics at an early stage for therapeutic purposes, the geometric mean titers of antibodies rose for 4-5 weeks after the bite was sustained. This led us to the tentative conclusion that it is possible to obtain reliable serological confirmation of new cases of Lyme disease by comparing the results of analysis of paired serum samples. It is desirable for one sample to be collected within the first days and the second, about 30 days after onset of the disease.

Thus, the first steps have been made in developing tactical procedures for diagnostic laboratory tests for borreliosis, refinement of which requires further research.

As noted above, circulation of *B. burgdorferi* in endemic sites of our country is linked to *Ixodes* ticks. Infected specimens have not been discovered as yet among the tested *Dermacentor reticulatus* from European USSR or *Haemaphysalis concinna* from the Far East, although some foreign data indicate positive findings for borrelia in representatives of the genera *Amblyomma*, *Dermacentor*, *Haemaphysalis* and *Rhipicephalus*. At the same time, incidence of infected adult, starving ticks of the genus *Ixodes* is rather high in endemic sites and, according to existing data, it reaches 30 for *I. ricinus* in

some areas and up to 50 percent or more for *I. persulcatus* [5, 8]. With reference to *I. ricinus* ticks, the possibility of transphase transmission of borrelia has been established experimentally [43, 46]. It has also been shown that, in principle, there can be transmission of *B. burgdorferi* from nymphs to imagoes of *I. persulcatus* without additional infection of the nymph phase by its source of nutrition. However, such transmission does not produce indicators of imago infection commensurate with the spontaneous level. In all likelihood, there is rather significant nymph infection in nature through blood-sucking [12]. Considering the polyzooid nature of the nymph phase of *I. ricinus* and *I. persulcatus*, it can be assumed that the epizootic process is sustained by many species of vertebrates, ranging from small mammals and birds to ungulates. Investigation of general patterns of pathogen circulation in endemic sites of Lyme disease and regional distinctions of their parasite systems is among our pressing and important tasks.

Since the prime route of transmission, as well as main vectors of Lyme disease and tick-borne encephalitis, are identical, the main epidemiological features of these infections (seasonal occurrence, causes and intensity of contact of the public with endemic sites, determining the occupational and age composition of Lyme disease victims, their distribution with respect to site of infection, etc.) are very similar. As in the case of tick-borne encephalitis, under present conditions the morbidity indicators are high among urban residents. The results of the first serological screening of the public, which we carried out, indicate that the intensity of contact with the pathogen is high. For example, almost 21 percent of serum samples taken from 730 residents of 2 pseudo-sites in Kirovskiy Rayon of Leningrad Oblast were positive in the nRIF with *B. burgdorferi* antigen, and in 9.7 percent of the cases, they were positive in dilutions of 1:40 or more. According to data obtained together with L. I. Moteyunas, 16 percent of the blue-collar workers in some rayons of Lithuania whose occupation is related to forests have antibodies. Since immunity to Lyme disease is not sterile, and the pathogen can persist for a long time in the body, there is reason to believe that some of the individuals with antibodies have the chronic form of this disease. For this reason, it is imperative to deploy in the immediate future a comprehensive study of the clinical spectrum of delayed and chronic manifestations of Lyme borreliosis, detection and laboratory confirmation of such cases, which would enable us to administer effective treatment to the patients.

What then is the incidence of Lyme borreliosis in our country and what is its place in contemporary infectious pathology? Only a strictly preliminary answer can be given to this question at the present time, on the basis of ideas concerning the breadth of distribution and epidemiology of the infection, level of vector infection and number of cases picked up in recent years in some regions. For example, in 1986-1988, in Leningrad Oblast alone (including the city) we verified about 250 new cases of Lyme disease among adult patients hospitalized

after sustaining a tick bite in medical institutions designated for such cases. Even these data, which are certainly far from complete, are 1.5-2 times higher than the number of cases of tick-borne encephalitis found there. In Sweden, which is relatively small in size and population, where *I. ricinus* and borreliosis are found only in the southern part of that country, more than 860 cases were serologically confirmed during the same years, while the indicators of intensity of morbidity constituted up to 40 per 100,000 people in different lans² [44]. This is about 5 times higher than the incidence of tick-borne encephalitis. On the basis of these data and some other information pertaining to countries of Central Europe, as well as the incidence of tick-borne encephalitis in recent years, we assume that there could be about 5000-7000 new cases of Lyme disease annually in our country and, consequently, this is by no means a rare infection. Apparently, it now holds a leading place among infections transmitted by ticks and one of the leading places among all endemic diseases of man. In essence, a new, independent major problem of infectious pathology has emerged, which requires appropriate attention on the part of the USSR Ministry of Health, research and methodological institutions, the sanitary and epidemiological service and attending physicians.

One of its many important aspects from the clinical point of view is related, on the one hand, to differential diagnosis of Lyme disease and tick-borne encephalitis and, on the other hand, the possibility of concurrent infection with virus and borrelia. Serologically verified cases of mixed infection in man are already known [8, 20]. We have demonstrated the existence of spontaneous infection of one tick specimen with pathogens of Lyme disease and tick-borne encephalitis by means of individual bacteriological and virological examination of adult *I. persulcatus* specimens from Khabarovsk Krai and comparison of our findings. According to estimates based on existing indicators of individual virus-carrying ticks and incidence of borrelia infection in them, the possible incidence of mixed infection of *I. ricinus* and *I. persulcatus* in different regions apparently fluctuates over a few percentage points, whereas in some areas it reaches 5-10 percent. In this regard, it is important to investigate the incidence of mixed infection in man, its early and delayed clinical manifestations, and the most effective treatment.

Thus, in the last few years investigation of Lyme disease began in our country. Virtually all scientific and organizational aspects of this major problem, some of which were mentioned above, require comprehensive work. In conclusion, we should like to mention the priority directions of research which, in our opinion are the key ones at this stage. They include, first of all, a need for immediate development of media for isolation and cultivation of borrelia based on ingredients produced in our country. This would permit not only unhampered field and laboratory studies of etiology, epizootiology and pathogenesis of borreliosis, but also accumulation of biomass of the pathogen sufficient to produce antigens in

the needed amounts. In other words, we will have a realistic opportunity for laboratory detection of Lyme disease on a national scale. At the first stages, it could be carried out by cultivating USSR reference strains of *B. burgdorferi* in regional bacteriological laboratories, producing corpuscular or soluble antigen for our own needs and testing serum at such laboratories (i.e., as is presently being done for leptospirosis, for example). At the same time, it will become possible to develop more technological and standard diagnostic agents.

Another important direction of work is the study of distribution of endemic sites of Lyme disease and extent of epidemiological hazard of areas. The most demonstrative indicator for this purpose is the incidence of infection of *Ixodes* ticks with borrelia, which can be detected relatively easily by dark-field microscopy of vital preparations or fixed smears stained after Giemsa. We have already refined the technique for making preparations and microscopy [4, 5], and there are no objective obstacles at the present time to such investigations.

We believe that in order to find a speedy solution to the most important aspects of the problem of Lyme disease in our country, it is imperative to devise a special comprehensive program, discuss and adopt it on the level of the USSR Ministry of Health and to provide special-purpose financing to different research and practical institutions for its implementation.

Footnotes

1. Reported to the 12th All-Union Conference on Endemicity of Diseases, Novosibirsk, October 1989.
2. Lan [with umlaut over the "a"] is the unit of administrative and territorial division in Sweden.

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UDC 577.21:579.871.1

Cloning and Expression of Diphtheria Toxin Gene and Gene Subunits in Escherichia coli

907C0032A Moscow *GENETIKA in Russian* Vol 26 No 6, Jun 90 (manuscript received 10 May 89) pp 990-999

[Article by M. M. Garayev, M. R. Bobkova, A. F. Bobkov, N. V. Lukashevich and Ye. V. Kazennova, Institute of Virology imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences, Moscow]

[Abstract] Production of diphtheria toxin in genetically engineered *E. coli* was secured by plasmid pBR322 transfer of BamHI fragments of ω -like tox^+ -corynephage $\phi 984$ of *Corynebacterium diphtheriae*. The diphtheria toxin gene was fully expressed in *E. coli* under its own regulatory resulting in the production of a 62 kD peptide possessing ADPP-transferase activity and reacting with specific anti-diphtheria toxin antibodies. The toxin was susceptible to *E. coli* proteases, with the substrate site located in the N-terminus region of the B subunit. Additional plasmids were constructed encoding for subunits A and B of the toxin, which led to the synthesis of A and B subunits suitable for construction of immunotoxins. Figures 4; tables 2; references 16: 4 Russian, 12 Western.

UDC 616.155.392.8-085.339:578.245

Recombinant α -Interferon (Reaferon) in Treatment of Chronic Myeloleukemia*917C0057A Moscow TERAPEVTICHESKIY ARKHIV in Russian Vol 62 No 7, Jul 90 pp 41-47*

[Article by N. D. Khoroshko, V. G. Savchenko, Ye. I. Kholopova, V. M. Kotel'nikov, A. V. Zakharova, Ye. A. Semenova, and V. I. Marchenko, All-Union State Science Center, USSR Ministry of Public Health, Moscow]

[Abstract] The search for new treatments for chronic myeloleukemia (CML) has attracted attention to the antiproliferative effect of interferons. The possibility of interferon treatment of CML patients appeared in 1987 with the development of domestic recombinant α interferon or reaferon, the powder with an activity of $0.5 \cdot 2 \cdot 10^6$ international units recommended for i/m use. Studies were performed using the same doses as are used abroad in the treatment of CML with this substance — 3 to $6 \cdot 10^6$ IU. Reaferon was administered to 46 CML patients from 17 to 51 years in age, 1 to 91 months after diagnosis. The medication was found to be well tolerated with few side effects and no negative influence on vitally important organs and systems. The studies found that the domestic reaferon has an independent antiproliferative effect and can be used in the treatment of CML. It is able to control the CML process without chemotherapy in the stable chronic phase of the disease, and is useful in combination with chemotherapy in the acute phase. References 27: Russian.

UDC 616.155.3:616.153.962.4-074:616.34-008.87

Influence of Leukocytic Interferon on Blood Kinin System in Patients with Acute Intestinal Infections*917C0064A Kiev VRACHEBNOYE DELO in Russian No 7, Jul 90 pp 109-111*

[Article by L. A. Trishkova, S. A. Kramarev, S. P. Nagornaya, M. A. Zimovets, A. A. Pashchenko, and I. K. Lisunkina, Department of Childhood Infectious Diseases, Kiev Medical Institute]

[Abstract] A study was performed of the dynamics of the kinin system in children with acute intestinal infections. The combination of biochemical methods was used, representing the activity of the kinin system and its inhibitors. Observations were performed on 102 patients with acute

intestinal infections, up to 1 year in age. The studies showed that during the acute period of intestinal infection there are manifest changes in the kinin system. It was found that interferon facilitates more rapid normalization of the kinin system in the patients when administered rectally. Symptoms of the infection and changes in the digestive tract also disappeared more rapidly with interferon administration. References 7: Russian.

UDC 615.38-015.4:612.017.1].036

Leukinterferon Immunostimulating Properties*917C0063A Moscow SOVETSKAYA MEDITSINA in Russian No 7, Jul 90 (manuscript received 6 Jul 89) pp 11-14*

[Article by N. D. Yushchuk, A. V. Zmyzgova, I. V. Tugutova, V. P. Kuznetsov, A. A. Babayants, T. A. Novikova, O. F. Yermmina, A. P. Mesnyankin, V. V. Lebedev, M. A. Vyushina, A. Ye. Kudryavtsev, and M. G. Kulagina, Chair of Infectious Diseases, MMSI [as published] imeni N. A. Semashko; Epidemiology and Microbiology Scientific Research Institute imeni N. F. Gamaleya, USSR Academy of Medical Sciences]

[Abstract] Leukinterferon, a new generation preparation consisting of natural interferon- α and cytokines, has been successfully employed in various bacterial infections. This paper presents the results of a comparative study of the effects of leukinterferon and recombinant interferon on 13 healthy people. The subjects were divided into three groups and were administered the preparations as follows: Group 1, leukinterferon, 10,000 IU, inhaled twice a day at 6 h intervals; Group 2, leukinterferon, 10,000 IU intramuscularly injected twice a day at 12 h intervals; and Group 3, recombinant interferon, 1,000,000 IU endolymphatically administered twice a day. The preparations were administered for 3 days during which time the subjects were carefully monitored. All groups tolerated the preparations satisfactorily without any toxic effects or allergic reactions noted. Group 1 subjects exhibited the best tolerance without any side effects other than a slight increase in temperature. Groups 2 and 3 experienced high temperatures, fatigue, and headache. The results demonstrated that leukinterferon activates the interferon status and stimulates cellular and humoral immunity, with T-lymphocytes shown to be the most sensitive. Leukinterferon is completely non-toxic when administered by inhalation or intramuscular injection. References 7: 6 Russian, 1 Western.

UDC 616-057-02:613.632]+616.98]-036.2-07

FON Data Base Monitoring System Designed To Determine Causes for Disease Outbreaks

917C0043B Moscow GIGIYENA I SANITARIYA in Russian No 6, Jun 90 (manuscript received 10 Mar 89) pp 45-47

[Article by B. N. Filatov and Ye. V. Bulanova, Hygiene, Toxicology, and Occupational Pathology Scientific Research Institute, USSR Ministry of Health, Volgograd]

[Abstract] The FON data base monitoring system is used on small computers to solve problems of determining the probability of causes of large-scale illness outbreaks in groups of people. It consists of 39 nosologic forms with the respective clinical symptomatics. Common as well as rare infectious diseases compose 54 percent of the total number of nosologic forms, while illnesses caused by organic chemicals compose the other 46 percent. The

program is written in DIAMS-2 language and consists of the basic program as well as 15 applied programs. The data to be entered include symptoms of the disease, description of the focal area, date the first patient became ill, number of patients at that moment, etc. The FON system was tested by verification with 60 cases of acute organophosphoric compound intoxication, with drug overdose patients serving as the control group. The FON system offered a correct diagnosis in 96.7 percent of cases, and an 11.6 percent false positive rate. A great deal of the difficulty in distinguishing illnesses with a chemical etiology from infectious diseases lies in the fact that clinical manifestations of intoxication have varying signs and symptoms as well as the fact that many of the same symptoms encountered in poisonings with chemicals also occur in infectious diseases. The findings suggest that the FON data base monitoring system may be very useful in diagnosing diseases of a chemical etiology. References 9: 2 Russian, 7 Western.

UDC 577.3

Effects of Low-Intensity Helium-Neon Laser Irradiation on Ethanol Production by *Zymomonas mobilis* Culture*907C0018B Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 312 No 4, Jun 90 (manuscript received 29 Nov 89) pp 990-992*

[Article by A. A. Timoshin and M. Ye. Beker, academician, Latvian SSR Acad. Sci., Institute of Microbiology imeni A. Kirkhenshteyn, Latvian SSR Academy of Sciences, Riga]

[Abstract] An analysis was conducted on the effects of He-Ne laser irradiation (632.8 nm; ca. 5 mW output; 0-50 min) on ethanol production by *Zymomonas mobilis* during 24 h of cultivation at 30°C on yeast-extract medium, pH 5.4. Control studies showed maximum ethanol synthesis in the 9-17 h period, with complete cessation by 24 h. Addition of 9 percent ethanol to the culture had an inhibitory effect. Trials with laser irradiation yielded a production pattern analogous to the control data, with essentially identical ethanol production with 1 to 50 min of irradiation. However, in cases with addition of ethanol to below inhibitory concentrations laser irradiation enhanced ethanol production by ca. 10 percent. The latter observations suggested that He-Ne laser action involved activation or repair of metabolic mechanisms impeded by addition of exogenous ethanol. Figures 1; tables 1; references 6: 4 Russian, 2 Western.

UDC 615.847.8.015.2:615.849.19].015.4

Biomechanism of Magnetolaser Therapy*917C0063B Moscow SOVETSKAYA MEDITSINA in Russian No 7, Jul 90 (manuscript received 2 Feb 90) pp 24-28*

[Article by V. Ye. Illarionov, Central Military Hospital imeni P. V. Mandryk, Moscow]

[Abstract] Magnetolaser devices have been produced since the mid- 1970s; however, there is no complete theoretical substantiation for the use of low energy laser radiation on a biological subject and no information on the combined methods of laser therapy. Therefore, a theoretical model of the biomechanism of a combined magnetolaser effect was constructed. It was shown that low energy laser radiation and a constant magnetic field combined are more powerful than low energy laser radiation alone, and spectroscopic splitting of the substance using a constant magnetic field expands the range for absorbing various wavelengths of light. As a result of combined magnetolaser irradiation of tissue, the atomic and molecular formation becomes excited, which enhances metabolic processes and aids in the appearance of free forms of the substance, biologically active products of photolysis, and a change in the pH of the environment. In addition, the energy activity of the cellular membrane changes, and conformational changes occur in the liquid crystal structure. It was also demonstrated that

various biological reactions occur as a result of physico-chemical processes. Studies on laser (635 subjects) and magnetolaser (311 subjects) therapy on patients with various pathologies (ischemic heart disease, hypertension, gastric ulcers, chronic bronchitis, etc.) demonstrated that combined constant magnetic field and low energy laser radiation is much more effective than low energy laser radiation alone, resulting in much more rapid healing. Figures 1; references 12 (Russian).

Use of Helium-Neon Laser to Accelerate the Generative Processes and Increase Training Effectiveness*917C0051A Moscow TEORIYA I PRAKTIKA FIZICHESKOY KULTURY in Russian No 7, Jul 90 pp 43-46*

[Article by N. D. Grayevskaya, T. I. Dolmatova, G. L. Shreyberg, S. D. Galimov, and N. I. Bliznets, Moscow oblast State Institute of Physical Culture; Central Scientific Research Institute of Sport]

[Abstract] Low-power laser radiation, usually provided by a helium-neon laser, has a biostimulating effect. This radiation causes expansion of dermal capillaries and increases the functional activity of cell elements, helps to cleanse injuries of microorganisms and accelerates wound healing, speeding epithelization, normalizing blood indicators. Laser treatment has a positive effect on degenerative trauma of the skeletomuscular apparatus, in vertebral osteochondrosis and various forms of cardiovascular pathology, particularly when applied to reflexogenous zones or biologically active points following the rules of acupuncture. The authors tested laser treatment in sports to improve performance, speed up recovery processes and normalize the condition of the body after physical training. Laser puncture was performed with a wavelength of 632 angstroms, power 10 mW, irradiated area 0.8 cm², irradiation time 3 minutes on each acupuncture point, total exposure time 8 minutes, each day for 10 days. Preliminary data indicate that all the athletes receiving laser puncture improved performance, recovered from training stress significantly more rapidly and adapted better to physical loads than the persons in the control group. References 8: Russian.

UDC 617-001.4-002.3-022.7-089:615.849.19]-
089.168-07:617-001.4- 008.87-078**Wound Process Description Following High Energy Laser Treatment and Enzymatic Therapy***917C0042A Moscow KHIRURGIYA in Russian No 6, Jun 90 (manuscript received 1 Dec 88) pp 12-16*

[Article by P. I. Tolstykh, A. I. Titov, Candidates of Medical Sciences Zh. S. Vartanyan, V. A. Derbenev, T. M. Danilova, and A. I. Dadashev, Laser Surgery Scientific Research Institute, Moscow]

[Abstract] The results of clinical and bacteriological investigations on 168 patients demonstrated that the use

of immobilized proteolytic enzymes significantly aids in maintaining the low level of microbial contamination achieved by CO₂-laser treatment of a wound and stimulates its healing. The CO₂-laser, one of the most promising means of treating purulent diseases and complications in surgery, can be used to resect and volatilize tissue and sterilize the wound and is much more effective than a scalpel in cleaning, but it does not provide the stable, prolonged sterilization obtained with immobilized proteolytic enzymes. Patients in Group 1 were treated with immobilized proteolytic enzymes following opening of the abscess while patients in Group 2 received debridement of the abscess using a CO₂-laser and local immobilized trypsin therapy. The results demonstrated that 19.7 percent of the control group, which received only conventional treatment, had secondary infections, while none were found in the experimental groups. Tests of antibiotic resistance of the microflora showed that they were very resistant to penicillin, ampicillin, meticcillin, and oxacillin, but 100 percent sensitive to amikacin and tobramycin. The findings also showed that the reduction of contamination was much more rapid in experimental groups, thereby resulting in shorter hospital stays and overall lengths of treatment. The optimal period for applying the secondary sutures in Group 1 was 5-7 days, while with patients in Group 2, surgery with CO₂-laser irradiation and enzymatic therapy may be the final stage of the operation. Accordingly, these findings indicate that immobilized proteolytic enzymes rapidly prepare the wound for applying the primary delayed suture or early secondary suture. Figures 3; tables 1; references 11 (Russian).

13486

UDC 617-001.4-002.3-084;615.849.19

Debridement With CO₂-Laser

917C0042B Moscow *KHIRURGIYA* in Russian No 6, Jun 90 (manuscript received 13 Oct 88) pp 16-18

[Article by G. D. Litvin, P. N. Nurmedov, V. A. Derbenev, and O. K. Kurbanova, Laser Surgery Scientific Research Institute, Moscow]

[Abstract] The potential for using a CO₂-laser in debridement of wounds as a means of preventing infection and improving the short and long term results of therapy was investigated on 20 3-4 kg male chinchilla rabbits. A 2x2 cm cutaneous wound was produced and subsequently infected with *Staphylococcus aureus*. Two hours later ten rabbits received debridement and wound sterilization with the Skalpel-1 CO₂-laser (10-15 W/cm²), while the second group of rabbits received only CO₂-laser treatment. Following an uneventful and identical healing process in both groups of rabbits, clinical trials were performed on 137 patients with cuts on the abdominal and thoracic walls and upper and lower limbs. Debridement with subsequent CO₂-laser therapy was performed on 68 patients, with later examination demonstrating a 95.7 percent rate of wound sterility. Sixty-nine patients received only CO₂-laser treatment and exhibited a 97.2 percent incidence of wound sterility. These results demonstrate that CO₂-laser treatment creates favorable conditions for early healing of the wound and for preventing serious complications. Accordingly, this CO₂-laser treatment has been recommended for widespread use throughout the country. References 5 (Russian).

13486

UDC 591.185.5

Electrophysiological Study of Hearing in Fresh Water Dolphin *Inia Geoffrensis*

907C0844c Moscow *DOKLADY AKADEMII NAUK SSSR in Russian Vol 313, No 1, Jul 90 (manuscript received 30 Nov 89) pp 238-241*

[Article by V. V. Polov, and A.Ya Supin, Institute of Evolutionary Morphology and Animal Ecology imeni A. N. Severtsov, USSR Academy of Sciences, Moscow]

[Abstract] The hearing of Amazon River dolphins was studied by recording the hearing induced potentials resulting from acoustic stimuli. The experiments were conducted in Peru on four animals, two males and two females. Needle electrodes placed 3-5 mm under the skin revealed that the response began in 0.1-1 msec, had an average

duration of 5 msec and a latent period of 0.7-0.8 msec. The form of the response was similar to that seen in other types of dolphins, with some differences. The earliest positive response peak was somewhat sharpened, and the amplitude of the entire response was greater, reaching 25 μ V in the most favorable cases. Threshold values were similar to those of other dolphin species. The dependence of response amplitude on stimulus intensity increased rapidly from 20 to 60 dB, more slowly from 60 to 80 dB, and then more quickly between 80 and 100 dB. The latent period decreased with increasing stimulus intensity. The slope of this dependence was greater than in other dolphins. The audiograms of the Amazon River dolphins had two minima, rather than one as seen in other dolphins and other mammals. Minimal thresholds were seen at 25-30 kHz and 70-80 kHz. Between these two areas the threshold increased by 25-40 dB. Response to rhythmic stimuli was similar to that seen in other dolphins. Figures 3; references 13: 7 Russian, 6 Western.

UDC 615.45

New Dressings Based on Natural and Synthetic Fiber Materials with Enzymatic and Antiseptic Effects

917C0055A Yerevan ZHURNAL
EKSPERIMENTALNOY I KLINICHESKOY
MEDITSINY in Russian Vol 30 No 1, Jan-Feb 90
pp 16-21

[Article by P. I. Tolstykh, B. N. Arutyunyan, A. Kh. Mukhtarov, and L. A. Mamedov, Scientific Research Institute of the Wood Industry; Razdan Central Regional Hospital]

[Abstract] Dressings with antiseptic and dehydration effect are useful in treatment of wounds. Urea, a universal proteinase inhibitor, does not inhibit immobilized proteinase. This article presents a study of the effectiveness of using dressing materials modified with proteinase, urea and antiseptics in the treatment of purulent wounds, demonstrating the desirability of their use considering the clinical situation and nature of the purulent-necrotic process. The preparation consisting of gauze with immobilized proteolytic enzymes—trypsin, urea and the antiseptic hibiton—is shown in experimental, clinical and cytologic studies to be an effective dressing for treatment of infected and purulent wounds, and can be recommended for use in clinical practice. References 4: Russian.

UDC 616.005.1-06:616.151.5-07

Expert System for Emergency Diagnosis of DIC Complications in Hemorrhagic Conditions

907C0041B Moscow SOVETSKAYA MEDITSINA in Russian No 6, Jun 90 (manuscript received 13 Jul 89) pp 89-92

[Article by V. S. Tsushko and A. N. Dubyaga, 'Sistema' Scientific Industrial Cooperative, Tyumen Medical Institute]

[Abstract] Cursory description is provided of an expert diagnostic system designed for DIC (disseminated intravascular coagulation) in various hemorrhagic conditions. The system consists of two parts, with the first based on analysis of 9 routine clinical symptoms indicative of DIC, with further differentiation into regional or systemic DIC. The system provides therapeutic recommendations and prognosis in case the recommendations are ignored by attending physician. The second component of the system relies on 13 clinical and paraclinical indicators for staging DIC and provides pathogenetic rationale for recommended therapy. Clinical usefulness of the system was demonstrated in a retrospective analysis of 36 cases with gastroduodenal hemorrhages and ten cases of postpartum bleeding complicated by DIC. References 5 (Russian).

UDC 616.61-089.843-06:[616.61-005.4-084]:[615.384:547.221]

Perfluorocarbon Emulsion Use in Kidney Transplant

917C0042C Moscow KHIRURGIYA in Russian No 6, Jun 90 (manuscript received 7 Dec 88) pp 98-103

[Article by N. A. Onishchenko, P. S. Sernyak, N. V. Kovalenko, D. I. Kalinin, P. A. Chernobrivtsev, and Ye. M. Berko]

[Abstract] The potential for using a perfluorocarbon emulsion (PFCE) blood substitute to prevent reperfusion damage to blood-deprived kidneys during autotransplantation was investigated on 18-26 kg dogs that were administered 15 mg/kg of PFCE. PFCE is an oxygen transport, antioxidant, membrane stabilizing agent that has been shown to aid in the more rapid restoration of the energy potential of the kidney and its metabolism. Animals that received PFCE exhibited an increase in the level of free-radical lipid peroxidation products in venous blood and tissue much lower than that of the control group. In addition, the experimental group showed a 62.3 percent increase in oxygen uptake and a 73.5 percent increase in ATP levels in the tissue. These were attributed to the oxygen transport and physicochemical properties of PFCE to increase the capillary gas-exchange area and oxygen delivery to the cells by many times. It was shown that reperfusion of blood-deprived kidneys with PFCE resulted in less activation of membrane degrading processes, thereby indicating that the PFCE blood substitute can be used to achieve enhanced normalization of the kidney transplant in the early post-operative period. In conclusion, the protective effect of the PFCE is due to a decrease in free-radical lipid peroxidation processes in membranes, creation of stronger conformational protein-lipid structures of the cell membranes, and normalization of oxidation-reduction and energy processes in renal tissue. Figures 2; tables 1; references 7 (Russian).

UDC 615.384:547.221].03:616.127-005.4-084

Preliminary Injection of Perfluoro Carbon Emulsion - A New Method to Protect Myocardium Against Ischemia

917C0076A Moscow BYULLETEN
EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 110 No 7, Jul 90 (manuscript received 25 Feb 89) pp 19-21

[Article by S. I. Vorobyev, Yu. V. Ladilov, V. V. Obratsov and G. R. Ivanitskiy, Institute of Biological Physics, USSR Academy of Sciences, Pushchino]

[Abstract] One effective way of protecting myocardium from ischemic and reperfusion damage is to inject prophylactically β -blockers, calcium antagonists, antioxidants, etc. Perfluoro compounds could be such potential agents for this purpose. In the present work, the effect of an injected emulsion of perfluoro carbons was investigated on the myocardium of rabbits. It was established

that injection of a proper dose of the emulsion at 1, 12 and 24 hours prior to experimental ischemia reduced the extent of ischemic and reperfusion damage to the myocardium. This effect was dose- and time-dependent. Figure 1; references 15: 14 Russian, 1 Western.

UDC
615.38.015.2:615.246.2].015.2:615.849.11].03:615.9.08

Physiohemotherapy in Comprehensive Detoxication of Body in Acute Exogenous Poisoning

917C0063C Moscow SOVETSKAYA MEDITSINA in Russian No 7, Jul 90 (manuscript received 26 May 89) pp 68-72

[Article by Ye. A. Luzhnikov, Yu. S. Goldfarb, M. M. Potshkveriya, M. V. Kutushov, Ya. I. Misulovin, Ye. V. Yastrebova, and O. V. Medvezhnikova, All-Union Center for Acute Poisoning Treatment; Emergency Aid Scientific Research Institute imeni N. V. Sklifosovskiy, Moscow]

[Abstract] Various artificial detoxication techniques (hemisorption, hemodialysis, and peritoneal and intestinal lavage) combined with ultraviolet irradiation or magnetic treatment of the blood were investigated as a means of enhancing detoxication effectiveness on 207 patients with second and third degree acute poisoning by organophosphoric compounds (133), psychotropic agents (66), and chlorinated hydrocarbons (8). Ultraviolet irradiation of the blood was performed on 138 patients using the MD-73M "Izolda" with a mercury-quartz lamp, 254 nm wavelength, for 20-60 min per session. Results indicated that ultraviolet irradiation was more efficacious on immunologic indices and needed to be conducted during and after operations to eliminate immunologic disturbances. Magnetic treatment of the blood was performed on 69 patients prior to hemisorption employing an electromagnet that created a heterogeneous 100 Hz constant or pulsed field in sessions lasting 30-60 min. Magnetic treatment was shown to be most effective when included in the preoperation preparation for the correction of hemorheologic disturbances, as indicated by the 30 percent increase in stroke volume and 8-15 percent increase in the hemoglobin and erythrocyte content of the blood within 1-7 days. Ultraviolet irradiation and magnetic treatment of the blood were employed when artificial detoxication techniques alone were insufficient and were shown to hasten the recovery rate, reduce the incidence of respiratory paralysis, shorten the duration of comas, and reduce the incidences of pneumonia and fatal outcomes. Accordingly, these findings demonstrate that ultraviolet irradiation and magnetic treatment of the blood should be included in physiohemotherapy to improve the outcome of acute exogenous poisonings. References 17: 14 Russian, 3 Western.

UDC 615.37.03:616.9-053.2].036

Interferon Therapy in Pediatric Infections

907C0086D Moscow VESTNIK AKADEMII MEDITSINSKIKH NAUK in Russian No 7, Jul 90 (manuscript received 20 Nov 89) pp 32-36

[Article by V. V. Malinovskaya and F. I. Yershov, Scientific Research Institute of Epidemiology and Microbiology imeni N. F. Gamaleya, USSR Academy of Medical Sciences, Moscow]

[Abstract] Initial studies on therapeutic applications of interferon in pediatric infections due to chlamydia, Gram-positive and -negative bacteria, and viruses (cytomegalovirus, herpesvirus, enterovirus) have shown that considerable benefit is to be derived from this form of immunotherapy, particularly when combined with vitamin E. Intrarectal administration of concentrated preparations of natural human interferon in combination with vitamin E in preterm and newborn infants has been shown to enhance α -interferon production 4.5-fold and γ -interferon 3-fold. Furthermore, the mortality rate in septic conditions was reduced to 16.7 percent versus 26.9 percent for conventional therapy. Preliminary clinical experience with recombinant α_2 -interferon, in combination with vitamins E and C, in 64 preterm and newborn infants with infectious processes has been positive in 93 percent of the cases. The therapeutic efficacy of this form of combination therapy has been attributed to the fact that both components, interferon and the antioxidant (vitamin E), serve to reinforce the immature immune mechanisms against the pathogenic microorganisms. Tables 3; references 24: 12 Russian, 12 Western.

UDC 616.36-036.12-085.361.438-036.8-07

Treatment of Chronic Liver Diseases with Thymalin and T-Activin

907C0041A Moscow SOVETSKAYA MEDITSINA in Russian No 6, Jun 90 (manuscript received 20 Jun 89) pp 85-88

[Article by O. I. Yakhontova, O. P. Dudanova and V. Kh. Khavinson, Chair of Propaedeutics in Internal Diseases, Petrozavodsk University]

[Abstract] Trials were conducted with two thymic preparations, thymalin and T-activin, in management of chronic liver diseases. The 37 patient cohort encompassed 12 cases of mixed micronodular cirrhosis, 16 cases of chronic active hepatitis, and 9 cases of chronic persistent forms of viral hepatitis. The patients were divided into two groups treated either with T-activin (100 μ g qd, i.m., x 5-8 days) or thymalin (10 mg qd, i.m., x 5-10 days). Both preparations were essentially equally efficacious, promoting a 15-16 percent increase in total lymphocytes within 7-10 days, as well as a 25-31 percent increase in T-lymphocytes, a 17.5 percent increase in monocytes and activation of macrophages. In addition, both preparations were particularly effective in chronic hepatitis with immune status improvement and diminished blood transaminase activity, gammaglobulin levels, and bilirubin. References 13: 11 Russian, 2 Western.

UDC 576.858.8

Infectious Titer of Phytopathogenic Bacteria and Its Practical Use

917C0053A Moscow *BIOLOGICHESKIYE NAUKI in Russian* No 7, Jul 90 pp 130-138

[Article by Ye. V. Matveyeva]

[Abstract] This article presents a review of the literature on the infectious titer of phytopathogenic bacteria and its practical use, discussing the concepts of the numerical threshold of infection, minimum effective dose, population and visible infectious threshold. There is in most cases the dose-effect relationship, often directly proportional regardless of whether quantitative or qualitative characteristics are used to measure the infectious titer. The results confirm the hypothesis of the independent action of each effective bacterial cell. In a few cases an ascending curve is observed, apparently indicating facultative synergism of the cells. The minimum effective dose for various pathogens is not over 5-30 bacterial cells placed directly on the plants. References 32: 3 Russian, 29 Western.

UDC 619:576.8.077.5

Specificity of Phage Typing of Listeria

907C0079A Moscow *VETERINARIA in Russian* No 7, Jul 90 pp 26-27

[Article by I. A. Bakulov, V. M. Kotlyarov, T. I. Kolpikova and N. A. Kapyrina, All-Union Scientific Research Institute of Veterinary Virology and Microbiology]

[Abstract] An analysis was conducted on the lytic activity and specificity of bacteriophages L2A and L4A to determine their suitability for phage typing of *Listeria monocytogenes*. Trials with 455 *L. monocytogenes* strains led to species

identification in 413 cases (90.7 percent), of which 363 belonged to serogroup I and 50 to serogroup II. Specificity was demonstrated by the fact that L2A and L4A did not lyse *L. murrayi*, *L. denitrificans*, *Erysipelothrix rhusiopathiae*, *Enterococci*, *Pasteurella*, *Corynebacterium*, *Streptococcus albus*, *Staphylococcus aureus*, *Escherichia coli* and *Salmonella*. Tables 1; references 6 (Russian).

UDC 579.843.95:579.25].08

Transduction of Chromosomal and Plasmid Markers by Bacteriophage P₁ in *Yersinia pseudotuberculosis*

907C0078B Moscow *MOLEKULYARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA in Russian* No 7, Jul 90 (manuscript received 15 Jun 89) pp 25-27

[Article by T. M. Stytsenko, M. I. Zarenkov and S. A. Lebedeva, Scientific Research Anti plague Institute, Rostov-on-Don]

[Abstract] Trials were conducted with a newly isolated bacteriophage P₁ clr100 cml to determine its suitability for chromosomal and plasmid transduction in *Yersinia pseudotuberculosis* 5504, as well as interspecies transduction between *Y. pseudotuberculosis* 5504 and *Y. pestis* EV76. The experimental approach relied on induction of auxotrophic mutants in the indicator strains. The results demonstrated that P₁ clr100 cml was effective in transducing individual chromosomal markers in *Y. pseudotuberculosis* 5504 with a frequency of 10⁻⁷ to 10⁻⁶/PFU. In addition, interspecies transduction in both directions involving chromosomal and plasmid markers was characterized by frequencies in the 10⁻⁸ to 10⁻⁶/PFU range. Consequently, the results demonstrated that P₁ clr100 cml is an efficient transducing agent in the *Yersinia* system. Tables 2; references 7: 5 Russian, 2 Western.

UDC 577.113.5

Localization of Smallpox Virus Gene Which Codes for 36K Major Membrane Protein

907C0846c Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 313, No 2, Jul 90 (manuscript received 2 Nov 89) pp 497-500

[Article by G. G. Prikhodko, N. V. Cheshenko, N. A. Netesova, Ye. N. Kozhina, A. V. Tetmenin, T. V. Lebedeva, E. G. Malygin, and S. K. Vasilenko, All-Union Scientific Research Institute of Molecular Biology, Koltso Settlement, Novosibirsk Oblast]

[Abstract] The results of the mapping of the vaccina viral gene which codes for the 36.4 kDa major membrane protein are presented. Total RNA was isolated from VNK-21 cells, the vaccina virus strain LIVP identified and isolated in the seventh hour of the infection cycle and selected by hybridization. The RNA was translated in a cell free system in the presence of ³⁵S-methionine. The translation products obtained contained a major protein with a molecular mass of 36 kDa. The results indicate that the open translation level 13 HindIII-F fragment of the vaccina virus gene undergoes transcription in the postreplication stage of viral infection. The protein possessed two terminal hydrophobic regions, of 16 and 30 residues, typical of membrane glycoproteins. A plasmid was constructed containing the sequence which codes for the open translation level product. Comparative analysis of expression of the chimeric protein was conducted in two E. coli strains. Expression was markedly greater in one strain than in the other. Positive results were obtained for the binding of the chimeric polypeptide with antiserum which was specific for the plasmatic membrane fraction. Viral protein from the plasmatic membrane of vaccina-infected VNK-21 cells was isolated and used to immunize rabbits. This produced an antiserum active against the 36.4 kDa major membrane protein. Results indicated that this protein is a component of infected cells and not the virion. Figures 4; references 15: 2 Russian, 13 Western.

UDC 577.112.5+577.113.5

Structural Determinants of Principal Myelin Protein Determining Sensitivity to Viral Infection. Cloning and Determination of Primary Structure of Principal Myelin Protein m-RNA in Adult Humans

907C0846b Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 313, No 2, Jul 90 (manuscript received 7 Aug 89) pp 494-497

[Article by V. A. Petrenko, A. A. Ilichev, A. I. Bedristov, N. N. Mikryukov, I. I. Krasnoborov, S. Ya. Golovin, S. I. Belikov, L. V. Mamayev, V. M. Blinov, and L. S. Sandakhchiyev, associate member, USSR Academy of Sciences, Scientific Research Design Technology Institute of Biologically Active Substances, Koltso Settlement, Novosibirsk Oblast]

[Abstract] A library of kDNA for adult human myelin was obtained and studied. By cloning the Pst-1 site in the pBR327 plasmid, 10,000 independent clones were produced, 5 percent of which hybridized with oligonucleotide probes for various myelin exons. The nucleotide sequence of seven of the clones was determined. Three of the clones coded for the 17.3 kDa protein, missing both the second and fifth exon, while the other four coded for the 18.5 kDa protein, missing only the second exon. Two of the clones coded for Tyr70 with TAC, while the other five coded for this residue with TAT. Previous work indicates that TAC predominates in embryonic myelin coding. The data indicate that humans possess two allelic genes for the principal myelin protein, both of which may be active in the brain of adults. The sequences found corresponded to those seen in the work of others, except that Ala25 was replaced by Tre25 and His78 was replaced by Asn78 in one clone, while Phe155 was replaced by Ser155 in another. Such variation, which may arise from somatic mutations, may explain differing susceptibility to postinfection autoimmune diseases. They may also be due to reverse transcriptase errors. Figures 1; references 6: 1 Russian, 5 Western.

UDC 578.832.1:578.5].08

Genome Structure of Influenza A/Leningrad/23/81 (H1N1) Virus

907C0078A Moscow MOLEKULYARNAYA GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA in Russian No 7, Jul 90 (manuscript received 27 Oct 89) pp 17-21

[Article by N. A. Petrov, Ye. B. Grinbaum, O. M. Litvinova, O. A. Gorbunov, I. A. Vtorushina, A. Ye. Nikulin, S. I. Belikov, S. K. Vasilenko, T. YA. Luzyanina and D. B. Golubev, 'Vektor' Scientific Industrial Association, All-Union Scientific Research Institute of Molecular Biology, Koltsovo, Novosibirsk Oblast; All-Union Scientific Research Institute for Influenza, USSR Ministry of Health, Leningrad]

[Abstract] An analysis was conducted on the primary structure of the genome of influenza virus A/Leningrad/23/81 (H1N1) isolated from the cerebrospinal fluid of a 1.5 year old child, who had been hospitalized with a diagnosis of 'suppurative meningitis.' Immunological, tissue culture, and sequencing studies revealed that 3 of the genes (M, PB1, PB2) showed marked homology with A(H1N1) viruses isolated in 1933-1941. The NA gene showed considerable similarity but not identity with the older isolates. The NS, NP and PA genes of A/Leningrad/23/81 (H1N1) were analogous to current A(H1N1) viruses in terms of primary structure, from which they apparently were derived via genetic reassortment. Accordingly, these findings indicate that A/Leningrad/23/81 (H1N1) represents an authentic antigenic anachronism. Tables 9; references 26: 8 Russian, 18 Western.

UDC 616.127-005.8-02:615.272.4.014.425

Emoxypine Antioxidant Effect on Necrotic Tissue Formation and Reparative Processes Following Myocardial Infarction

917C0061A Moscow KARDIOLOGIYA in Russian Vol 30 No 7, Jul 90 (manuscript received 27 Oct 89) pp 50-53

[Article by A. P. Golikov, V. L. Ovchinnikov, V. Yu. Polumiskov, B. V. Davydov, V. A. Karev, L. A. Konorev, and A. A. Shvedova, Emergency Aid Institute imeni. N. V. Sklifosovskiy, Moscow]

[Abstract] The effect of emoxypine, a new, water soluble antioxidant that is a structural analog to vitamin B₆, on the formation of necrotic tissue and reparative processes following myocardial infarction was investigated on 70 patients with primary large focal myocardial infarction admitted to the hospital less than 6 h following the onset of the attack. In addition to the symptomatic therapy that the control group received, the experimental group also received 10 mg/kg of emoxypine per day for 5 days intravenously, followed by 1 mg/kg intramuscularly for 15 days. Clinical observations made using an electrocardiogram to compare changes between the two groups demonstrated that emoxypine therapy limited the size of the necrotic area, leaving more viable myocardium. Trials performed on male Wistar rats that were administered 10 mg/kg of emoxypine every day following myocardial infarction demonstrated that the relative mass of the right ventricle as compared to the left ventricle increased in control animals, whereas the opposite was true in experimental animals. The results demonstrate that emoxypine normalizes peroxide oxidation of lipids, accelerates collagen synthesis in post infarction scars, and improves microcirculation by inhibiting fibrin-forming processes and delaying aggregation of thrombocytes, in addition to dilating coronary vessels. Furthermore, signs of post-infarction cardiac insufficiency are less frequently observed in patients treated with emoxypine. These data, in addition to the significantly lower mortality rate (6.7 percent versus 17.6 percent) observed among the experimental group, suggest that emoxypine is ready for greater clinical use. Figures 2; tables 1; references 15: 11 Russian, 4 Western.

UDC 616.137.8/9-007.272-085.31:547.943:547.95]-036.8-07

Pathophysiological and Clinical Evaluation of Dalargin Efficacy in Management of Occlusive Arterial Diseases of Lower Extremities

917C0061B Moscow KARDIOLOGIYA in Russian Vol 30 No 7, Jul 90 (manuscript received 30 May 89) pp 77-79

[Article by G. K. Zoloyev, V. A. Dudko, G. Ye. Sokolovich, V. D. Poyarkov, V. I. Ponurovskiy, M. E. Beloglazov, N. P. Ivatsin, N. A. Stepanyan, and M. G. Shilnikov, Cardiology Scientific Research Institute, Tomsk

Scientific Center, USSR Academy of Medical Sciences; Novokuznets Branch, Central Scientific Research Center of Prosthetics]

[Abstract] Dalargin, a synthetic enkephalin analog with a broad spectrum of action, has been used in the treatment of myocardial infarction, ischemic heart disease, and arterial hypertension due to its ability to diminish tonus and total peripheral resistance, decrease cholesterol levels, and reduce ischemia. Accordingly, dalargin's effect on the pathogenesis and clinical course of occlusive arterial diseases of the lower extremities was studied on 87 male patients with endarteritis and occlusive atherosclerosis of lower limb arteries. The results demonstrated decreases in lactate, cholesterol, and parathyroid hormone levels 7 days after patients began treatment, and showed that the group that received dalargin earlier improved more quickly than the group that was administered a placebo for 5 days before receiving dalargin. Dalargin's beneficial effect is attributed to more rapid and effective improvement of endocrine and metabolic indices that consequently prevent ischemic damage to tissue. Tables 2; references 17: 13 Russian, 4 Western.

UDC 615.339:578.245].012.7:612.821.2].07

Synthesis and Mnemonic Effects of Interferon Fragments 43-49 and 121-125

907C0037A Moscow
KHIMIKO-FARMATSEVTICHESKIY ZHURNAL in Russian Vol 26 No 6, Jun 90 (manuscript received 14 Jun 89) pp 30-33

[Article by O. S. Papsuyevich, G. I. Chipens, V. A. Krauz, A. L. Drozdova, M. Yu. Galushko and T. A. Petrov, Institute of Organic Synthesis, Latvian SSR Academy of Sciences, Riga; Dnepropetrovsk Medical Institute]

[Abstract] Peptide fragments 43-49 (I) and 121-125 (II) of interferon - α 2 were synthesized by conventional protein chemistry and tested for their mnemonic and cardiovascular effects vis-a-vis arg-vasopressin. Trials on 150-200 g Wistar rats showed that intraperitoneal administration of 20 μ g/kg of I resulted in recovery of extinguished passive avoidance response in 25 percent of the animals within 30 min, with recovery seen in 43.8 percent of the animals in 2 h. The recovery figure reached 38-39 percent after 30 min with 4-10 μ g/kg of peptide II. The effects of both fragments on memory were equivalent to those obtained with arg-vasopressin. However, peptide I and II were devoid of meaningful cardiovascular effects in outbred 5-10 kg dogs, while arg-vasopressin decreased the heart rate and elevated blood pressure for approximately 60 min. Tables 2; references 4: 3 Russian, 1 Western.

UDC 615.339:578.245].012.7:612.821.2].07

Screening Diphenyldi(aryloxy)silanes for Anti-Inflammatory Activity

907C0037B Moscow

KHIMIKO-FARMATSEVTICHESKIY ZHURNAL in Russian Vol 24 No 6, Jun 90 (manuscript received 1 Aug 89) pp 33-34

[Article by A. D. Dzhurayev, K. M. Karimkulov, A. G. Makhsumov, U. B. Zakirov, Sh. D. Radzhabova and N. Kh. Tsinzadze, Tashkent Medical Institute]

[Abstract] A group of 14 diphenyldi(aryloxy)silanes were synthesized and tested for anti-inflammatory properties in a rat model relying on histamine-induced arthritis in a posterior extremity. In a dose of 25 mg/kg every agent displayed weak activity in alleviating edema, with the efficacy increasing with a further increase in dosage (50-150 mg/kg). In terms of efficacy the agents ranked as follows: Cl > I > Br; with o-Cl > p-Cl, o-Br > p-Br > 2,4-Br₂, and p-I > m-I > o-I. Substitution of OH for the halogen atoms resulted in a 34.2 percent reduction in activity. Diphenyldi(2,4-dichlorobenzoyloxy)silane was the most potent agent, reducing edema by 40.3 percent when administered in a dose of 150 mg/kg and comparing favorable with the 26.2 percent reduction obtained with 100 mg/kg phenylbutazone. Toxicity studies on 18-23 g mice showed no deaths with 2800 mg/kg of the agents administered subcutaneously, whereas the LD₅₀ value for phenylbutazone was 430 mg/kg. Tables 2; references 2 (Russian).

UDC 615.451.234:577.352.2]:615.324:665.211].012

Ectericid as Dispersant for Liposomal Drug Forms

907C0040A Moscow VESTNIK AKADEMII

MEDITSINSKIKH NAUK in Russian No 6, Jun 90 (manuscript received 3 Apr 89) pp 40-44

[Article by I. L. Dikiy, L. S. Strelnikov, V. I. Chuyeshov, V. D. Yakovenko and A. D. Bazavluk, Pharmaceutical Institute, Kharkov]

[Abstract] Ectericid, an antibacteria product of fish fat, was employed as a dispersant for antibiotic-bearing lecithin liposomes designed for clinical testing. The liposomes were shown to be 490 nm in diameters with an internal volume of 1.60 mg/g, resistant to lyophilization (96 percent), heat and pH (98°C and ca. 2.0 for 50 percent destruction, respectively). Treatment of tonsillar crypts with antibiotic-loaded liposomes (incorporating rifampicin in the membranes and encapsulating gentamicin) in a dosage of 10 mg/ml 5-7 days before tonsillectomy reduced the preoperative bacterial counts to 2000 CFU/ml from a control value of > 10⁸ CFU/ml. The liposomes displayed tropism for erosive areas creating an antibiotic depot at the site of lesion. In addition, the combination of ectericid with the antibiotics created a

synergistic combination which potentiated the effects of the antibiotics 63- to 1173-fold. Tables 3; references 14 (Russian).

UDC 615.276:[615.451.234:547.953].07

Anti-inflammatory Action of Liposomes

907C0040B Moscow VESTNIK AKADEMII

MEDITSINSKIKH NAUK in Russian No 6, Jun 90 (manuscript received 3 Apr 89) pp 44-47

[Article by V. M. Kreys, V. M. Melnikova, Ya. M. Margolin, L. P. Melyantseva, A. I. Gladshteyn and B. A. Andriasyan, Laboratory of Biomedical Problems, Kemerovo Medical Institute]

[Abstract] Mature, 150-200 g, Wistar rats were employed in tests conducted on the anti-inflammatory properties of liposomes prepared in a conventional manner from egg phosphatidylcholine and cholesterol. The results demonstrated that subplantal administration of 0.15 ml of liposomes (25-50 mg/ml) 1 h before subplantal injection of 0.1 ml of 2 percent formalin attenuated edema formation by > 50 percent at 4 h. Another study involved s.c. administration of the liposomal preparation (100 mg/kg) into the shank area 1 h before s.c. injection of 0.5 ml of 9 percent acetic acid into the femur, and then 50 mg/kg q. 4 days until the wound healed. Necrosis developed at the site of acetic acid injection in 2-3 days; however, in liposome-treated animals the area of the lesion was ca. 50 percent smaller in comparison with the size in control animals. After 6 days the differences were less pronounced and healing was completed in ca. 25 days in both groups. Finally, tube dilution studies with *Staphylococcus aureus* 209P and *E. coli* M-17 at 30°C for 27 h yielded minimum effective concentrations of 3.1 and 6.2 mg/ml, respectively. Accordingly, these observations demonstrated that liposomal preparation in question possesses anti-inflammatory and antibacterial actions, and presumably acts via membrane mechanisms. Figures 4; references 21; 14 Russian, 7 Western.

UDC 575:579.252.5:579.841.31

Synthesis of Antisense RNA and Inhibition of Chloramphenicol Acetyltransferase (CAT) in Transgenic Tobacco Plants

907C0018A Moscow DOKLADY AKADEMII NAUK

SSSR in Russian Vol 312 No 4, Jun 90 (manuscript received 29 Dec 89) pp 981-983

[Article by I. F. Kanevskiy and F. Nod, Institute of Botany imeni N. G. Kholodnyy, Ukrainian SSR Academy of Sciences, Kiev; Institute of Plant Physiology, Biological Research Center, Hungarian Academy of Sciences, Szeged]

[Abstract] Regulation of gene expression by synthesis of antisense RNA was achieved in transgenic tobacco (*Nicotiana tabacum*, Havana strain, SRI mutant) leaf discs transformed by a novel binary vectors. The system under consideration involved depression of CAT activity in plants infected with agrobacterium bearing a binary vector (F-60) capable of ensuring transcription of large quantities of antisense CAT-RNA. The results revealed that under optimum conditions CAT activity was reduced 10-90 percent. However, there was no direct correlation between the degree of CAT inhibition and transcriptional efficiency of the antisense gene. The key observation consisted of demonstration of the feasibility of regulating gene expression in transgenic tobacco plants, findings that may be particularly useful in cases of lethal mutations. Figures 3; references 14 (Western).

UDC 616-008.922.1-008.64-092.9-085.273.53:547.953]
.014.6:615.451.234:577.352.2]-036.8

Biologic Effects of Liposomes in Hypoxic States

907C0040C Moscow VESTNIK AKADEMII
MEDITSINSKIKH NAUK in Russian No 6, Jun 90
(manuscript received 3 Aug 89) pp 47-51

[Article by A. V. Stefanov, V. P. Pozharov, T. D. Minyaylenko, S. A. Bryginskiy, M. M. Seredenko and V. K. Lishko, Institutes of Biochemistry imeni A. V. Palladin and of Physiology imeni A. A. Bogomolets, Ukrainian SSR Academy of Sciences, Kiev]

[Abstract] Phosphatidylcholine liposomes were tested for their therapeutic efficacy in 150-200 g male Wistar rats subjected to three model hypoxic conditions. Hypoxia was induced by either inhalation of a gas mixture containing 6 percent oxygen, hemorrhage (2-2.5 ml/100 g), and induced pneumonia. In the first case the animals were treated i.v. or intratracheally with 2.5 mg/100 g of liposomes within 30 min, and in the second case treatment was limited to the i.v. route. In the pneumonia model treatment consisted of inhalation of liposomes (qid, x 4 days), commencing 4 days after induction of pneumonia. Treatment was effective in reducing the mortality in hypoxic hypoxia from 60 percent in the control animals to 18 percent in the treated animals; oxygen uptake increased by 20-30 percent, oxygen tension in arterial blood increased from ca. 67.4 to 83.4 mm Hg, and blood lactic acid fell 2- to 3-fold. In addition, lactic acid accumulation in various tissues and organs fell by 45 (brain) to 70 percent (skeletal muscles), and lipid peroxidation in internal organs was reduced 2- to 3-fold. The antioxidative properties of phosphatidylcholine as a factor in limiting lipid peroxidation were facilitated by utilization of excess NAD formed by glycolysis as indicated by the sharp drop (1.4- to 1.7-fold) in the blood lactate/pyruvate ratio following administration of the liposomes. In the final analysis, these observations demonstrated that liposomal treatment affected all factors involved in pathogenesis of hypoxic changes. Figures 1; references 21: 15 Russian, 6 Western.

UDC 612.014+577.352.315

Potential Gated Oxytocin Channels in Functional BLM-Smooth Muscle Plasma Membrane' Complex

907C0031B Kiev DOKLADY AKADEMII NAUK UKRAINSKOY SSR: SERIYA B—GEOLOGICHESKIYE, KHIMICHESKIYE I BIOLOGICHESKIYE NAUKI in Russian No 8, Aug 90 (manuscript received 14 Mar 89) pp 73-76

[Article by V. K. Rybalchenko, G. V. Ostrovskaya, A. M. Omelchenko and A. V. Pastukh, Institute of Physiology, Kiev State University]

[Abstract] To further define the mechanism of action of oxytocin, the effects of oxytocin on azolectin bilayer lipid membrane (BLM) and BLM-plasma membrane complex (BLM-PMC) were subjected to electrophysiological measurements. Oxytocin was shown to bind firmly to the lipid components of BLM and BLM-PMC with formation of Ca^{2+} channels having a lifetime ranging from 3 to 45 sec. Application of a negative potential (50-120 V) to the side subjected to the peptide had virtually no effect on the channels, while a positive potential decreased the lifetime in a potential-related manner. At +100 mV the Ca^{2+} channels became closed. These observations lend themselves to the interpretation that at rest, when the membrane potential is positive, oxytocin-dependent channels are closed and the Ca-pump is functional. As the plasma membrane of the smooth muscle cell is excited and the potential reverses the oxytocin-dependent channels open and the Ca-pump becomes inactivated. Accordingly, the effects of oxytocin are dependent on the state of excitability of the plasma membrane. Figures 1. references 7: 6 Russian, 1 Western.

UDC 591.881:591.185.6:591.044.6

Tuftsins-Induced Morphometric Changes in Visual, Sensorimotor and Nucleus Accumbens Neurons

907C0594A Leningrad TSITOLOGIYA in Russian Vol 32 No 1, Jan 90 (manuscript received 28 Mar 89) pp 41-46

[Article by T. L. Chebotareva, Scientific Brain Research Institute, USSR Academy of Medical Sciences, Moscow]

[Abstract] Intraperitoneal administration of 300 µg/kg of tuftsins to 180-200 g outbred male rats was shown to induce selective changes in the visual, sensorimotor and nucleus accumbens neurons over a 60 min period of observation. The changes consisted of a decrease in cytoplasmic protein of projection and efferent neurons in layers IV and V of the visual cortex during the first 30 min, followed by recovery to baseline levels in 60 min. An increase in protein levels in layer III of the visual cortex was first noted 50 min after tuftsins administration. In layer V of the sensorimotor cortex an increase in the cytoplasmic area and protein content reached a plateau in 15 min. A concomitant increase in protein concentration and cytoplasmic area in layer III appeared

to represent cumulative mechanisms rather than an actual increase in protein synthesis. Within 15-30 min of tuftsins injection neuronal size and protein concentrations in n. accumbens increased to stable levels that persisted for 60 min. The observations were interpreted to indicate that greater plasticity is displayed by neurons of layers IV and V of the visual cortex and n. accumbens than by layer V of the sensorimotor cortex and associative neurons of layers III of the visual and sensorimotor areas. In addition, the results demonstrated that morphometric studies may be used to derive information about the plasticity of the various formations. Figures 3; references 9: 8 Russian, 1 Western.

UDC 615.384:547.221].017:615.246.2].015.4:612.123].076.9

Composition of Lipids Absorbed by Emulsions of Some Perfluoroorganic Compounds During Circulation in Blood Stream

917C0077A Moscow KHIMIKO-FARMATSEVTICHESKIY ZHURNAL in Russian Vol 24 No 7, Jul 90 (manuscript received 20 Nov 89) pp 16-18

[Article by Ye. V. Tereshina and N. N. Doronina, All Union Scientific Research Institute TKGP (unknown abbreviation - abstractor), Moscow]

[Abstract] The synthetic emulsifier, one of the surface active agents, known in the USSR under the name of "proxanol" is included in most of the perfluoroorganic compounds (PFC) currently produced for medicinal use; it is a block-copolymer of ethylene oxide and propylene oxide. It stabilizes PFC in vitro preventing its coalescence. It was noted that up to 30 percent of injected proxanol could not be identified in blood samples, suggesting that it was bound to PFC. Yet, in spite of this, the emulsion continued to circulate in the dispersed form. An assumption was made that this stability of the emulsion was due to the formation of a new absorption layer on PFC particles consisting of proxanol and various lipids, since it was already shown that a mixture of perfluorodecaline and perfluorotripropylamine (PFD/PFPA) was indeed absorbing various lipids. The composition of lipids absorbed by perfluoroorganic compound emulsions was studied using the following emulsions: PFD, PFPA and perfluoroparamethylcyclohexylpiperidine stabilized with P-268 (PFMCHP). It was shown that PFD emulsion absorbed primarily phosphatidylcholine (PC - about 50 percent) and sphingomyelin (SM - 30 percent one hour after infusion, dropping to 7 percent after 24 hrs). Among the common lipids, cholesterol (Ch) reached 50 percent of their total level. A similar pattern was observed with PFPA. In case of PFMCHP, PC and SM levels were 36 and 33 percent respectively, phosphatidylethanolamine - 16 percent and phosphatidylserine - 14 percent. Among the absorbed common lipids, Ch, triglycerides and free fatty acids corresponded to 25, 14 and 12 percent respectively. This

absorptive property of PFC should find practical use in cardiology. References 4: 2 Russian, 2 Western.

UDC 615.31:547.979.733].03:616-008.922.1].07

Antihypoxic Properties of Meso-Substituted Porphyrines

917C0077B Moscow

KHIMIKO-FARMATSEVTICHESKIY ZHURNAL in Russian Vol 24 No 7, Jul 90 (manuscript received 31 Jul 89) pp 43-45

[Article by V. I. Melnik, S. E. Sharapova, Z. I. Zhilina and T. V. Stoletova, Odessa University imeni I. I. Mechnikov]

[Abstract] A number of 5,10,15,20-substituted porphyrines were synthesized and their structure-antihypoxic activity relationship was investigated under conditions of hemic hypoxia and hypercapnic hypoxia. Following R- were substituted on 5,10,15 and 20 positions: phenyl, 3,4-methoxyphenyl; 2,3-benzo-1,4-dioxo-2-cyclohexen-4-yl; 2,3-benzo-1,4-dioxo-2-cyclopenten-4'-yl; 2,3-benzo-1,4,7,10-tetraoxa-2-cyclododecen-4'-yl; 2,3-benzo-1,4,7,10,13-pentaoxa-2-cyclopentadecen-4'-yl and 2,3-benzo-1,4,7,10,13,16-hexaoxa-2-cyclooctadecen-4'-yl. All of these compounds exhibited activity only under conditions of hypercapnic hypoxia induced in the hermivolume. The most pronounced antihypoxic effect was noted in the porphyrin containing a heliotropic residue. All of them were found to be of great interest as enhancers of body's resistance during hypoxic conditions. Crown porphyrines are capable of binding alkali and alkaline-earth metal cations (K^+ , Ca^{2+}) and so they may be used as models for the study of membrane transport processes during the development of abnormal conditions such as hypoxia. References 7: 5 Russian, 2 Western.

UDC 616-001.17-06[616.98:579.861.2]-
092.9-06;616.12-008.6-084:[615.31:547.95:547;943

Restriction of Functional Disorders by Means of Regulatory Peptide - Dalargin in Burned Rats Injected With Staphylococcus Aureus

917C0076B Moscow BYULLETEN

EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 110 No 7, Jul 90 (manuscript received 6 Jul 89) pp 24-26

[Article by S. B. Patushin, Institute of Surgery imeni A. V. Vishnevskiy, USSR Academy of Medical Sciences, Moscow]

[Abstract] The goal of this work was to investigate the capability of the synthetic analog of an opioid neuropeptide - dalargin to increase the resistance of rats to infection with Staphylococcus aureus after exposure to burn trauma. Dalargin is an endogenous neuropeptide, D-Ala²-Arg⁶-leu-enkephalin modified to increase its biological effect and resistance to proteolytic enzymes. It

was shown that the results of burn trauma are manifested by serious functional disorders in the myocardium, high frequency of the development of gastric ulcers and depressed ability of an organism to fight microbial toxemia. Dalargin is capable of correcting these problems by limiting or entirely blocking the damaging effect of burn trauma and by preventing the development of infectious complications. References 5: 4 Russian, 1 Western.

UDC 612.438-577.15/.17

Neuron Sensitivity to Serotonin Allosterically Stimulated by Thymopentin

917C0025A Riga IZVESTIYA LATVIYSKOY

AKADEMIJ NAUK in Russian No 8, Aug 90 (manuscript received 24 Apr 90) pp 115-119

[Article by A. T. Dolzhenko, V. Ye. Klusha, and N. A. Kharin, Donetsk Medical Institute; Organic Synthesis Institute, Latvian Academy of Sciences]

[Abstract] Prompted by the search for new psychotropic agents, especially among thymic hormones that have been found in high concentrations in the nerve endings of many subcortical structures of the brain, the effect of thymopentin, a neuropeptide that has exhibited stress protection and anxiologic properties in behavioral and neurochemical tests, was investigated on nerve cell function in isolated brain tissue. Comparative studies have demonstrated that the anxiologic properties of thymopentin equal diazepam in effectiveness, and that like diazepam, thymopentin increased the content of gamma aminobutyric acid (GABA) and serotonin in brain homogenates. Accordingly, in order to determine how thymopentin acts specifically, the III-V lumbar spinal ganglia of adult rats were isolated to analyze the neuronal effects of serotonin (5-hydroxytryptamine). It was demonstrated that different neurons of sensory ganglia respond to 5-hydroxytryptamine with three types of reactions: slowly developing and rapidly developing depolarization with an increase in membrane resistance, and hyperpolarization accompanied by an increase in membrane conductance. Subsequently, the hyperpolarization response was investigated with calculation of the ability of buspirone and the buspirone-like agonist serotonin MJ 13653 to induce 5-hydroxytryptamine-like hyperpolarization. These findings suggest that the hyperpolarizing effect is due to an increase in K^+ permeability of neuron membranes, while the hyperpolarizing effect of 5-hydroxytryptamine is associated with a decrease in intracellular cAMP. In contrast to 5-hydroxytryptamine and buspirone, thymopentin does not alter the neuron membrane potential in 15 min superfusion of the sensory ganglia with saline solution containing thymopentin at 10^{-7} - 10^{-5} mol/l concentrations. The ability of thymopentin to alter the effects of 5-hydroxytryptamine and serotonin agonists suggests that stimulation of the hyperpolarization effects of 5-hydroxytryptamine and GABA mimetics is due to thymopentin's effect on IA type

serotonin receptors and GABA_B receptors, but occurs by an allosteric mechanism, as thymopentin itself does not alter the membrane potential of neurons and does not reproduce the effects of 5- hydroxytryptamine and GABA mimetics. The findings suggest that this possibly occurs because the serotonergic mechanisms become involved in the anxiologic effects of thymopentin as a

means of altering GABA- ergic control of 5- hydroxytryptamine-ergic neurons of the midbrain nuclei that help carry out the anti-anxiologic effect of 5- hydroxytryptamine agonists, as well as being a result of the direct allosteric effect on 5-hydroxytryptamine-sensitive neuron membranes. Figures 1; tables 1; references 12: 4 Russian, 8 Western.

UDC 614.876+612.014.481

Health Care of Belorussian Population in Connection With Accident at Chernobyl Nuclear Power Plant

907C0862A Minsk ZDRAVOOKHRANENIYE
BELORUSSII in Russian No 6, Jun 90 pp 3-8

[Article by S. Ulashchik [BSSR Minister of Health at time of accident]]

[Text] The accident at the Chernobyl Nuclear Power Plant is the greatest disaster in the entire history of development of atomic energy. The extent, quality of contamination and particularly its medical sequelae continue to be defined, and at present they are the subject of heated discussions, not only in our country but, as I learned first hand, also abroad. The only thing that is not questioned is the sad fact that a significant part (up to 70 percent) of the territory contaminated with radionuclides is contained in our republic.

Brief Description of Postaccident Radiation Situation

As a result of the explosion of the nuclear reactor and its active zone, a large amount of products of nuclear fission and induced activity was released: radionuclides of krypton, xenon, iodine, cesium, strontium, ruthenium, americium, cerium, plutonium and other chemical elements. Overall activity of discharges due to the accident is estimated at 5×10^7 Ci, or about 3-4 percent of total activity of products of nuclear fission in the reactor [1]. Some scientists consider these figures to be too low [4]. The shares of activity discharged because of the accident were approximately as follows: 20 percent iodine-131, 13 percent cesium-137, 10 percent cesium-134, whereas the figures for most other isotopes range from 2 to 5 percent, including 4 percent for strontium [1].

Iodine isotopes are considered to be the main dose-forming and, consequently, biologically significant short-lived radionuclides and cesium and strontium are so considered among long-lived ones [3]. The contribution of plutonium isotopes requires combined evaluation.

Fallout of radioactive substances on the territory of the USSR following the Chernobyl accident occurred mainly in three large spots: the Ukraine, Belorussia and western oblasts of RSFSR. Of all fallout in the world, 19 percent of iodine-131 and 11 percent of cesium-137 lie in Belorussia. In BSSR, about 18 percent of the farmland was contaminated with radionuclides. For this reason, 256,000 ha of farmland, including 79,300 ha of plowed fields, were excluded from agricultural use.

The following factors affected formation of the radiation situation: prolonged (10 days) leakage from the reactor of radioactive flow enriched with isotopes of cesium; nonuniform removal from the atmosphere of radioactive isotopes that rose as part of the gas and aerosol current to different altitudes; change in direction of migration of

the radioactive block due to difficult meteorological conditions and steps that were taken.

The process of development of the terrestrial wake of the radioactive cloud differed appreciably from the conceptions of its formation in the case of a nuclear explosion or even of instantaneous discharge from a reactor. Hence the difficulty in assessing the radiation situation, delayed identification of different contaminated territories and unsatisfactory information given to the public, and occasionally making some hasty decisions. All this had an adverse effect on the psychoemotional climate among the public and caused distrust in official information and competent agencies.

The effects of the accident-caused radioactive contamination of the environment on people is attributable mainly to three sources: radioactive cloud, gamma radiation from radionuclides that fell on the ground and their penetration into the body with food and water, and to a lesser extent with air when breathing.

At first, the structure of the projected 50-70-year dose was viewed as follows: about 15 percent dose of external irradiation, 85 percent internal radiation (provided local foodstuffs were consumed). Thanks to steps that were taken, the ratio of doses of external to internal radiation is actually 1:1, and it is expected to be 60 and 40 percent in 50 years [1]. The level of radioactive contamination and type of soil may change the structure of irradiation of the public.

The following figures are indicative of the enormous impact of the accident on Belorussia. About 2.2 million people living in Gomel, Mogilev, Brest, Minsk and Grodno oblasts, where contamination of soil with cesium exceeds 1 Ci/km^2 are exposed to radiation. More than 102,000 people, including about 30,000 children, reside in areas where cesium-137 contamination constitutes 15 Ci/km^2 or more.

The radiation situation at the present time is characterized by relative stability, but it is not safe. The rates at which the gamma background and environmental contamination are declining have slowed down appreciably, as compared to the initial post-accident period, and this requires correction of forecasts.

Chernobyl Accident-Related Work of Public Health Agencies and Institutes

The Belorussian Ministry of Health, oblast and rayon health care agencies and institutes are constantly concentrating on the medical and health aspects of the Chernobyl AES [nuclear power plant] accident. Thanks to a large extent to the efforts of practicing physicians and public health organizers it was possible to minimize the impact of the accident and lower its adverse effects on inhabitants of this republic. Medical workers have had to learn and readjust as they proceeded, along with the entire population.

What then has the BSSR Ministry of Health and its agencies specifically accomplished at the sites in the postaccident period?

1. A system of management and coordination of activities of public health agencies and institutions was organized to render medical aid to the public residing in radionuclide-contaminated territories. The work is implemented by: functionaries at the BSSR Ministry of Health (deputy minister), at oblast health departments (deputy chief), at TsRB [central rayon hospitals] (deputy chief physician); department for eradication of sequelae of Chernobyl AES accident; Republic Special Dispensary and Republic Center for Personal Dosimetry, departments of oblast and rayon hospitals. At the present time, oblast centers of radiation medicine have been organized at some oblast hospitals in the cities of Gomel and Mogilev. A coordinating council headed by the minister monitors their work. Shortly after the accident, additional physicians and mid-level medical personnel were furnished to medical institutions of involved regions.

The Radiation Medicine NPO [scientific and production association], which includes laboratories and departments of all scientific research institutes of the BSSR Ministry of Health, provide scientific support of the work on the medical impact of the accident. The chief institution is the Belorussian Scientific Research Institute of Radiation Medicine, which was founded in May 1988.

2. From the first days after the accident, there was organization of monitoring of the radiation situation in the republic, primarily of radioactive contamination of foodstuffs and water. More than 1.5 million tests of foodstuffs and water were carried out in 1986-1989. The results of the readings indicate that the percentage of samples exceeding the MPL [maximum permissible level] is declining from year to year. Drinking water contained cesium in amounts exceeding the MPL only in the first year after the accident. At present, the BSSR Ministry of Health has submitted a proposal for a stricter MPL for cesium and setting them for strontium. True, the possibilities for testing the latter are quite limited for the time being.

3. One of the focal tasks was and still is to develop and implement measure to lower dose burdens on the public. In order to determine them, human pulse counters have been installed in all regions with high radioactivity and the relevant service was founded. More than 30,000 personal dosimeters are in use.

The following steps were carried out with the participation of medical workers:

- 24,700 people were evacuated from 107 populated centers in the first year after the accident, and they are under regular medical supervision;
- there is annual decontamination of populated centers in strictly monitored zones, but because of the limited and incomplete nature of the work and poor disposal

of contaminated soil the efficacy of decontamination is low, and it must be improved;

- the supply of foodstuffs conforming to the MPL has been set up properly;
- in the zones of high radioactivity, a set of farmland-improvement measures has been carried; since 1989 the permissible level of nitrates in farm products has been lowered; steps have been taken to regulate toxic chemical use in contaminated territory;
- the scope of work to improve the health of mothers and infants, pregnant women, school children and adults residing in contaminated territories is growing from year to year; for example, more than 57,000 children have been treated in 1989, and it is planned to treat more than 190,000 people in 1990, including about 93,000 children; apparently, it is opportune to recall that, already since 5 May 1986, mass-scale screening was begun of residents of involved regions, and in that period more than 500,000 people were examined (361,000 in Gomel Oblast); thyroid and liver tests were carried out on more than 143,000 people (26,000 children), and in the first month after the accident 11,682 people were hospitalized (5751 children).

Thanks to these and other protective measures, radiation doses to the public were lower than predicted and than those that could have prevailed were it not for the postaccident steps taken.

The overall mean dosage of external and internal radiation to which the public was exposed in regions of strictly monitored zones constituted about 6.5 rem in 1986-1989; it was 10.1 rem in the region with cesium contamination in excess of 40 Ci/km², whereas with a contamination level of 15-40 Ci/km² it was 3.8 rem. Mean exposure dose for 1989 was 0.76 rem. Of course, these data do not take into full account exposure to all isotopes that fell on the territory of this republic. Here too, there is something for researchers of all ministries and agencies to work on.

The radiation doses would have been smaller if sanitation requirements and special precautionary measures had been followed more strictly in the home and at work, particularly in agriculture.

People who were exposed to doses exceeding the postaccident limit set for that period (17.3 rem) require special attention. Even the most conservative estimates indicate that there are more than 3500 such people in this republic (not counting those involved in the postaccident cleanup).

We should dwell in particular on the dose burdens to the thyroid. The difficulty of the situation is that considerable groups of children and adults residing in regions endemic for goiter who did not receive appropriate preventive iodine treatment either before or after the accident, were exposed to iodine radionuclides. According to reports (N. Ye. Savchenko, 1986), it is only on 30 April 1986 that preventive iodine treatment was begun, and it covered only 150,000 residents of Gomel Oblast, including more than 36,000 children.

According to the preliminary data of the Scientific Research Institute of Biophysics, USSR Ministry of Health, the dosage to the thyroid gland could exceed 200 rad considerably in a rather large part of the children from regions that are the most contaminated with radionuclides. As we know, such radiation doses can cause changes in the thyroid gland. Today there are already signs of formation of thyroid pathology: aggravation of endemic goiter, higher incidence of autoimmune thyroiditis, formation of risk groups for hypothyroidism, etc. [2].

4. The work done by clinical institutions in regions exposed to radionuclide contamination is basically to provide dispensary care of the residents of these areas. Dispensary care coverage is provided for virtually all those in strictly monitored zones. But the quality of dispensary care and health-improving measures is not always satisfactory. Things are worse for those involved in cleanup following the Chernobyl accident. In spite of repeated requests, information about them is incomplete and furnished with delay to public health agencies and institutions.

5. Establishment of the All-Union distribution register holds a large place in the work of the BSSR Ministry of Health and its institutions. It must contain long-term automated individual records on people exposed to ionizing radiation, their children and subsequent generations, as well as radiation doses, evaluation of health status and its changes. The BSSR Ministry of Health and its regional computer and data processing center were asked to design this register on the republic level, and this was accomplished by the appropriate target date. However, due to improper filling out of forms and lack of appropriate programs on the oblast and rayon levels, proper use of the register has been delayed.

As of 1 January 1990, information pertaining to 173,400 people in Belorussia has been entered in the register; this includes 17,900 adults evacuated from the 30-km zone and 37,400 children.

6. Support in terms of medical personnel continues to evoke much criticism. Manning medical institutions with physicians and mid-level medical personnel is worse now in several rayons of Gomel and Mogilev oblasts as compared to 1985. As of today, there are still 1149 vacancies for physicians and 1669 for mid-level medical personnel. This is so, in spite of the priority referral to these regions of graduates of medical VUZ's and schools, constant invitation of physicians from other regions of our country, offering various preferential benefits to medical personnel, etc. As before, we are compelled to call upon clinical residents, the staff of clinical scientific research institutes and visiting brigades from less affected parts of this republic and the city of Minsk to work in these rayons. In recent times, the Belorussian Ministry of Health is experiencing major difficulties in manning visiting teams.

We must mention the following among the major steps carried out by the ministry in order to improve support, in terms of medical personnel of this republic, for the stricken regions:

- transfer of the Vitebsk Medical Institute to the jurisdiction of the BSSR Ministry of Health;
- increased enrollment (as compared to 1985) in medical VUZ (by 300 people) and medical schools (by 1230 people);
- opening four affiliates (Chechersk, Zhlobin, Klimovichi, Molodechno) of medical schools;
- organization of special enrollment of students in medical institutes of this republic (in recent years, 330 places were allocated for Gomel Oblast, 285 for Mogilev Oblast and 100 for Brest Oblast);
- suggestions have been made pertaining to preferential benefits for medical personnel working in regions contaminated by radionuclides, as well as to establish a Chernobyl medical fund.

In addition, an affiliate of the Vitebsk Medical Institute is being opened in the city of Gomel, whereas a premed department was opened at Gomel University for residents of Gomel and Mogilev oblasts.

Much attention is also being given to professional training of medical cadres: resident-training has been organized for physicians in hematology, endocrinology and oncology. Specialists in radiation medicine are being trained on special graduate-student programs. In 1990, there will be two cycles of instruction in radiation medicine at the Belorussian Institute for Advanced Training of Physicians; physicians are being sent for the same purpose to train in the cities of Kiev and Lvov. There is absolutely no doubt that such work requires further development and improvement. Students at medical VUZ are obviously receiving inadequate training in radiation medicine at the present time.

7. The accident at the Chernobyl AES has required priority supply of medical equipment to the stricken regions. This is being done in accordance with the concept of technical retooling of this sector. However, because of inadequate additional allocation of medical equipment by the USSR Ministry, this problem had to be resolved by the BSSR Ministry of Health by means of redistribution of such equipment to different oblasts. For this reason, it is only by 1990 that it was possible to meet more or less satisfactorily the demands of medical institutions concerning radiometry apparatus and different diagnostic instruments. In the first half of this year, all regions with high radioactivity, as well as the scientific research institutes working on this problem, will be provided with ultrasound and endoscopic apparatus. By the end of this year, it is planned to resolve this matter with respect to laboratory equipment, primarily hematological, and to furnish the necessary reagents.

The industrial enterprises of this republic have started to put out medical equipment.

8. The problem of priority drug supply for stricken regions has been resolved in an analogous manner. Thus far, the decision of the board of the USSR Ministry of Health dated 21 October 1988 concerning centralized supply of drugs to these regions has not been implemented. In spite of the difficulties, the BSSR Ministry of Health and its Pharmacy Association succeeded in 90-95 percent delivery on requisitions of medical institutions in contaminated regions, whereas the figure for the entire republic is 70-75 percent.

9. Speedy improvement of the material and technical base of health care is very important to lowering the adverse sequelae of the accident at the Chernobyl AES. It is planned to spend about 900 million rubles for construction and reconstruction of health care facilities in stricken regions. Only 25.7 million rubles was allocated for 1986-1989. In the postaccident period, 7 hospitals with a total of 616 beds, 5 polyclinics handling 1700 visits per shift, 56 rural medical walk-in facilities with a total of 117 beds, which can handle 3290 visits per shift, and 311 FAP [feldsher-midwife centers] have been built.

10. The Chernobyl accident required a radical change in the subject matter of research at scientific research institutes and VUZ's under the BSSR Ministry of Health. This work became more systematic after the Scientific Research Institute of Radiation Medicine was founded and the Radiation Medicine Scientific and Production Association was organized there. The

research deals with assessment of biomedical sequelae of the Chernobyl accident and development of methods to prevent them.

Many of the research projects served as the basis for adopting a number of organizational measures, and validating the 1990-1995 State Program for Eradication From BSSR of the Sequelae of the Chernobyl Accident. Yet we cannot fail to admit that, thus far, obviously insufficient use is being made of the potential of medical science in this republic, with respect to resolving the biomedical aspects of the Chernobyl accident.

11. For all these years, the BSSR Ministry of Health has devoted much attention to explanatory and health-education work with the republic's inhabitants, mainly in the stricken regions. It must be stated that this work did not yield the expected results. A search must be made for new ways and means of working with the public and, mainly, for speedy implementation of all measures outlined in the State Program, including the voluntary move, in stages, of inhabitants from the contaminated territories.

General Description of Health Status of Inhabitants of Belorussia in the Postaccident Period

As can be seen from the data listed in the table, the medical-demographic indicators did not undergo noticeable change, whereas some of them, for example, infant and maternal death rates, even demonstrate positive dynamics. There have been no marked changes in the structure of causes of death among the population and infant mortality. We can merely point to some rise in deaths due to neoplasms (148.2 per 100,000 population in 1985, 156.9 in 1987 and 169.4 in 1989).

Medical-demographic health indicators for BSSR population

Indicator	City of Minsk	Oblast						BSSR	USSR
		Brest	Vitebsk	Gomel	Grodno	Minsk	Mogilev		
Mortality/1000 population									
—1985	6.0	10.6	12.4	10.3	12.0	12.1	11.3	10.6	10.6
—1987	5.8	9.9	11.3	9.8	11.0	11.6	10.4	9.9	9.9
—1988	6.0	10.0	11.6	10.1	11.2	11.8	10.4	10.1	10.1
—1989	6.4	10.1	11.5	10.1	10.9	11.3	10.9	10.1	10.0
Infant mortality/1000 births									
—1985	13.4	14.2	14.3	16.3	12.1	16.1	14.2	14.5	26.0
—1987	14.4	12.5	13.4	14.1	12.2	14.7	11.9	13.4	25.4
—1988	14.0	11.6	13.4	12.4	11.2	16.1	13.0	13.1	24.7
—1989	13.3	11.2	12.4	11.8	10.6	11.9	10.2	11.7	22.3
Disability, work days/100 workers									
—1985	—	555.1	711.6	576.2	674.3	797.4	648.0	690.7	869.0
—1987	—	558.4	682.0	680.6	573.8	787.6	602.9	677.5	813.0
—1988	—	650.6	787.2	776.9	653.7	931.4	685.0	785.6	901.9
—1989	—	632.1	761.8	790.0	658.6	888.1	687.0	770.6	888.4

The BSSR Ministry of Health is being accused very unfairly of complacency and concealment of the true situation. It is simply a matter of having a discriminating and dialectical attitude toward such information. We believe that the stable medicodemographic indicators are more indicative of being conservative and of a rise in general level of health care, rather than absence of impact of the Chernobyl accident on the health of people in this republic. The following information concerning the incidence of different diseases, which started to rise in 1988-1989 is also in favor of such an interpretation.

A rise in incidence of anemia and chronic ENT diseases was noted in 1989 among the child population. Mean annual rise in incidence of iron-deficiency anemia is in the range of 20 to 40 percent. In 1989, the highest morbidity was observed in contaminated rayons (Krasnopol'skiy, Cherikovskiy and Slavgorodskiy) of Mogilev Oblast. However, the incidence of chronic diseases of the throat and nose was highest in rayons of high radioactivity in Gomel Oblast. In addition, there was reliable rise in incidence among children of acute respiratory viral infections, chronic bronchitis, bronchial asthma and pneumonia in a number of the stricken regions.

There has also been a rise in morbidity among the adult population of the rayons under observation. The most distinct rise was noted in incidence of hypertensive disease and peptic ulcers, ischemic heart disease, cerebrovascular pathology, osteoarthritis, chronic bronchitis and others. Laboratory changes in the immune system were found in almost one-third of the tested people in different age groups. The epidemic situation for tuberculosis is not improving in regions with high radioactivity.

There is a trend toward rise in incidence of leukemia, primarily chronic forms of hemoblastosis. In some regions there has been a rise in acute leukemia among children. We were impressed by the wave-like shape of the leukemia incidence curve.

Let me touch upon the question of possible genetic sequelae of the Chernobyl accident. Among such consequences, the most significant is the increase in number of infants with congenital developmental defects. According to data of scientific research institutes, the incidence of such defects has risen from 4.27/1000 births in 1984-1985 to 6.89 in 1987-1988 in the 17 most contaminated rayons of Gomel and Mogilev oblasts. In 1989, this indicator dropped to 5.62, and became the same as before the accident in this republic and for the first years after it. The incidence of developmental defects in aborted fetuses is higher in the same rayons (11.6 \pm 2.3 percent) than, for example, in the city of Minsk (5.6 \pm 0.3 percent) and city of Mogilev (4.3 \pm 0.8 percent). There must be further development and improvement of teratological research. Even more attention should be devoted in this republic to the medicogenetic service, particularly prenatal diagnostics.

Tasks for Health Care Agencies and Institutions in the Next Few Years

The State Program of BSSR demonstrates rather clearly the direction of work of the Belorussian Ministry of Health, its agencies and institutions dealing with eradication of the sequelae of the Chernobyl AES accident.

Work on the BSSR register of distribution must be completed in the immediate future; this is an information-controlling system, the most important tasks for which are to investigate morbidity among the people under observation, its link to dose loads, and automated monitoring of implementation of therapeutic and preventive measures.

Public health agencies and scientific institutions of this republic must quickly prepare some methodological documents, according to which one could analyze morbidity in radionuclide-contaminated rayons and determine its cause-and-effect relationship to the effects of different factors. Such methodological recommendations are very necessary to the work of both practicing physicians and the Republic Interagency Commission concerned with determination of the link between morbidity and disability, on the one hand, and the Chernobyl accident, on the other.

It is extremely important for the sanitary and epidemiological service of the BSSR Ministry of Health, along with other concerned ministries and agencies, to take exhaustive steps to prevent (or minimize) the spread of radionuclides over this republic. This means a gradual change to consumption of clean foods, discontinuation of production of contaminated goods, reliable burial of radioactive waste. There should be discussion, as a future research and practical task, the problem of maximum removal of radionuclides from the republic's contaminated regions, using the achievements of worldwide scientific and technical progress to accomplish this.

One of the reasons for the unsatisfactory solution of a number of problems of eradication of biomedical sequelae of the accident is the shortage of qualified manpower in the area of radiobiology and radiation medicine. For this reason, under such conditions, it is rather important not only to accelerate the training of highly qualified personnel, but to unite all institutions working under the Belorussian Ministry of Health, BSSR Academy of Sciences and BSSR Ministry of Public Education on the Chernobyl problem into a single scientific, educational and practical center of radiation biology and medicine.

There is an extremely large task to be accomplished for radical improvement of medical services to individuals involved in eradicating the consequences of the accident at the Chernobyl AES. To this day, not all of them are on the records, many undergo dispensary care irregularly and are not treated promptly.

In the years since the accident, attention was focused mainly on people residing in regions with cesium contamination in excess of 15 Ci/km². Less attention has been given to those living in less contaminated regions. As it was learned, the health indicators and dose burdens for these groups are occasionally worse than for people in the monitored rayons. It is quite apparent that the steps to eradicate the consequences of the Chernobyl accident (including medical and sanitation) must also be extended to regions with low levels of radioactive contamination. And this needs to be done very soon.

Everyone attributes much importance to treating people residing in radionuclide-contaminated areas. However, there are many oversights in organization of health-improving measures, and in a number of instances their efficacy remains low. For this reason, preparation of scientifically validated recommendations for treatment at sanatoriums and resorts, as well as rest homes for individuals from the stricken regions is an important task for the Belorussian Ministry of Health and Belorussian Trade-Union Council.

Thus, time is making some serious adjustments in our conceptions of the extent of the Chernobyl accident and its biomedical sequelae. They turned out to be much more serious and diverse than suspected in the first years following the accident. A collective effort is needed for utmost reduction of the adverse effects of the nuclear accident on the population of Belorussia and, first of all, the health of the present and future generations. It is only through the active work of all ministries and agencies and conscientious assistance of the public that the State Program can be executed, and that is the least that must be done in the existing situation. I want to hope that health care agencies and institutions, and all medical workers of Belorussia are ready for this long-term, difficult and responsible, but extremely necessary work for the Belorussian people.

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UDC 614.876:621.039.586(476)

The Ecological Radiation Situation and Biomedical Aspects of Sequelae of the Accident at the Chernobyl Nuclear Power Plant in Belorussia

907C0862B Minsk ZDRAVOOKHRANENIYE
BELORUSSII in Russian No 6, Jun 90 (manuscript
received 26 Mar 90) pp 8-11

[Article by V. A. Matyukhin, Academician of the USSR Academy of Medical Sciences, Belorussian Scientific Research Institute of Radiation Medicine]

[Text] The unprecedented scope of the Chernobyl accident determined the ecological and biomedical distinctions of its consequences.

As we know, many tens of millions of curies (Ci) of radioactive substances were discharged into the environment. The highly radioactive gas-and-aerosol spill from the reactor's active zone continued for 10 days. For the cleanup, a number of materials and compounds were placed in the reactor's active zone, and they were also dispersed by heat flow.

The main biologically significant radionuclides resulting from the accident, particularly within the first few days, were iodine isotopes. These nuclides formed dose loads to the human and animal thyroid gland for 2-3 months after the accident. Among the long-lived radionuclides, radioactive cesium and strontium had the deciding impact on the radiation situation.

The territory of Bryansk, Kiev, Zhitomir, Gomel, Mogilev and Brest oblasts were contaminated. There are some small spots in Minsk and Grodno oblasts. The breakdown of fallout is as follows: 10 percent ¹³¹I and 11 percent ¹³⁷Cs in BSSR; 20 and 6 percent, respectively in northern UkSSR; 12 and 7 percent in the Central Economic Region of RSFSR, 14 and 18 percent in the rest of European RSFSR; 1 and 2 percent, respectively, in the Asian part of the USSR, 28 percent ¹³¹I and 38 percent ¹³⁷Cs in Europe (with the exception of the USSR), 6 and 18 percent, respectively, for the rest of the world [6].

Of the total fallout in our country, 70 percent is the share of BSSR with contamination in excess of 15 Ci/km². A total of 2.2 million people, which is 20 percent of the total population of this republic, reside in areas of Belorussia with contamination in excess of 1 Ci/km², and 18 percent of the farmland is contaminated. There are 102,000 inhabitants, including about 30,000 children in the most affected zone (over 15 Ci/km² in Gomel and Mogilev oblasts).

At the present time, the radiation situation involves long-lived ^{137}Cs , ^{134}Cs , ^{90}Sr , ^{239}Pu and ^{240}Pu radionuclides. Cesium radionuclides make the predominant contribution to the radiation dose. As for strontium and plutonium, their role in irradiation of the body as a whole is assessed as insignificant, as compared to radio-cesium, but this does not preclude the need for planned and in-depth investigation of their effects on man in the case of prolonged and constant contact.

The distinctions of the ecological radiation situation in Belorussia are determined by the following features: —contamination of large territories in the republic, which was already mentioned above; —nonuniform, patchy and spotty distribution of contamination, even within the same populated center and adjacent areas, which creates additional difficulties in dosimetric monitoring and, consequently, assessment of actual dose loads on each person; —differences in spectrum of fallout of radionuclides and combinations thereof; —biochemical distinctions of soils in contaminated areas, resulting in different coefficients of radionuclide migration into plants and then (over food chains) into man; for this reason, a correlation does not always exist between density of contamination of an area and levels of radionuclide accumulation in people residing in these regions; —even before the Chernobyl accident, there had been radioactive fallout in this republic, as indicated by the results of studying levels of radioactive strontium in people and intake of radionuclides in food [2, 8].

In assessing the impact of radionuclides on health of the population after the accident, one must consider two time periods. The first was notable for the effects of short-lived radionuclides (up to 2-3 months after the accident), when ^{131}I , which produced a substantial load to the thyroid (biological chain: soil—plants—dairy cattle—man), was the deciding factor in the radiation effects. External irradiation (remote) and the inhalation route made a smaller contribution. The second period is characterized by the effects of long-lived radionuclides, mainly cesium and strontium, both as a result of intake with food and external γ -radiation.

After the accident, the USSR Ministry of Health put into effect an emergency standard for maximum permissible concentration of ^{131}I in milk (3700 Bq/liter), which corresponded to a thyroid dose load of 0.3 Sv [Sievert] (30 rem) in children. Thanks to the measures implemented for radiation protection of the public, primarily to prevent or minimize intake of ^{131}I , it was possible to lower the potential dose loads by 50-80 percent.

Formation of the dose load is slower under the effect of radiocesium and it is characterized by lower absolute values. Unlike an "iodine" load, where we are dealing with local irradiation of a critical organ, the thyroid, radiocesium irradiates the whole body.

As the radiation and genetic situation was clarified in the stricken regions, it became necessary for the first time in radioprotection practice to make validated decisions as

to possibility of living in contaminated areas considering the exposure forecast. The hypothesis that there is no threshold of action of ionizing radiation as it applies to undesirable effects of exposure, i.e., it is assumed that any radiation dose does not preclude the possibility of long-term adverse aftereffects, served as the theoretical basis for such decisions. In our country, the overall dose that an individual can be exposed to over a lifetime, as the degree of risk of long-term stochastic effects, was proposed as a tentative criterion for making decisions as to relocating inhabitants. After thorough analysis, the National Committee for Radiation Safety recommended a dose of 0.35 Sv (35 rem) over a 70-year lifetime. This dose range also includes the doses to which the public was exposed since 26 April 1986 [1, 5].

However, in BSSR, on the level of government decisions these requirements are stricter and the idea is advanced of expediency of relocating inhabitants from areas where contamination density is low, but where it is impossible to raise clean agricultural products. In such cases, it is recommended to relocate families with children up to the age of 14 years, pregnant women and individuals for whom medical indications prohibit living in contaminated areas. A broad spectrum of radiation-control measures, which was developed by world and Soviet science, was and continues to be implemented to lower radiation exposure of the people of this republic. A total of 24,700 people were evacuated from 107 populated centers and they received preventive iodine therapy; land-improvement and decontamination measures are being carried out constantly, as well as work on delivering water to populated centers; a supply of clean foodstuffs is provided for the public, those residing in contaminated regions are being treated, and other steps are being taken.

The set of preventive and decontamination measures carried out in the monitored regions has lowered to 2/5ths (of the previous level) the dosage of external radiation and to 1/10th-1/15th that of internal exposure.

The cumulative radiation dose to which residents of the "strict monitoring" zone (where superficial activity constitutes $\geq 15 \text{ Ci/km}^2$) was exposed averaged about 5.9 rem; it was 9 rem for areas with density of cesium contamination in excess of 40 Ci/km^2 and less than 3.4 rem elsewhere. Consequently, the actual exposure doses were substantially lower than the standards set for the period of the accident (15.5 rem over the indicated period). However, mean radiation exposure dose reached the accident level in some populated centers.

We are distressed and concerned mainly about the fate of children whose thyroid was exposed to radioactive iodine in doses exceeding 200 rem.

Since the accident, health agencies focused their attention mainly on the following tasks:

—monitoring the radiation situation and doing everything they could to lower the radiation load on the public;

- providing dispensary care for the public and administering appropriate treatment to the different population groups;
- establishment of the All-Union distribution register for dynamic monitoring of the health status of people exposed to radiation and their offspring;
- radical improvement of the material and technical base of health care in Mogilev and Gomel oblasts;
- carrying out research.

Different scientific research institutes in the system of the BSSR Ministry of Health began to investigate the medical aspects of the accident. The scattered nature of research, absence of effective coordination of investigations raised the question of the need to organize a scientific research institute of radiation medicine in Belorussia.

The Belorussian Scientific Research Institute of Radiation Medicine was founded on the basis of a decree dated 5 March 1988 of the Central Committee of the Communist Party of Belorussia and BSSR Council of Ministers. This institute concentrated research related to investigation of the medical and ecological aspects of the accident at the Chernobyl AES. It was confirmed as the chief institution in the system of the BSSR Ministry of Health dealing with problems of radiation medicine.

In January 1989, the clinic based at the former Aksakovshchina Sanatorium, which included a specialized pediatric dispensary as a dispensary-polyclinic department, was placed under the jurisdiction of the Belorussian Scientific Research Institute of Radiation Medicine. At the present time, this institute has four working bases that are 40 km apart. It is planned to build a complex for the institute in the settlement of Novinka.

Affiliates of this institute have been opened in the cities of Gomel and Mogilev, and the question of opening an affiliate in the city of Vitebsk is under consideration.

In June 1989, the Radiation Medicine Research and Production Association, which comprises both scientific research institutes and clinical health care institutions, was established in the system of the BSSR Ministry of Health.

The Belorussian Scientific Research Institute of Radiation Medicine is working in two main directions:

- investigation of distribution of radionuclides in food, routes of their penetration into the body, assessment of exposure doses received and predicted for residents of this republic, and elaboration of measures to lower these doses;
- comprehensive evaluation and prognosis of health status of inhabitants of monitored regions of BSSR, elaboration of scientific bases for dispensary supervision and production of the register; development of

methods for diagnosing and correcting any detected disturbances caused by radiation.

The institute is the chief institution for Section 9.2 of the National Program for Eradication From Belorussian SSR of the Consequences of the Chernobyl AES Accident in 1990-1995: "Development and adoption of a system for assessing health status of inhabitants of territories contaminated with radionuclides, definition of safe living and working conditions, development of methods for diagnosis, prevention and treatment of diseases and determination of the effects on the body of low doses of radiation and combined effects."

On the basis of the results of investigations carried out in 1989 at the Belorussian Scientific Research Institute of Radiation Medicine, it was learned that internal cesium level diminished by more than a factor of 10, as compared to 1986, and was 1/3-1/2 the 1987 level. It was established (in Gomel Oblast) that, depending on density of soil contamination with cesium, mean ^{137}Cs levels in adults were as follows: 0.26 $\mu\text{Ci/person}$ in zones with contamination density of 1-5 Ci/km^2 , 0.69 μCi with 5-15 Ci/km^2 , 0.91 μCi with 15-40 Ci/km^2 , 1.10 μCi with 40-60 Ci/km^2 and 1.68 $\mu\text{Ci/person}$ in zones of over 60 Ci/km^2 [4].

Levels of radioactive substances in children and adolescents are one-half to one-fifth the adult level and does not exceed 0.3 $\mu\text{Ci/child}$. The levels of radioactive substances depend on the extent to which restrictions on intake of contaminated food were obeyed, as well as extent of migration of radionuclides from soil into plants and then over the food chains into man.

In virtually all regions with ^{137}Cs contamination density of 1-5 Ci/km^2 there may be some people and entire populated centers exposed to mean annual radiation dose that exceeds 0.5 rem, which is the maximum allowed by the radiation safety standard. For this reason, it is necessary to organize universal dosimetry of inhabitants in the entire region contaminated with radionuclides [3].

It is imperative to impose restrictions on consumption of locally produced food regardless of density of contamination in the area in all of the recorded populated centers with expected annual dose of 0.5 rem or more.

Analysis of forecasts of possible stochastic sequelae of whole-body exposure of the inhabitants of contaminated regions enables us to conclude that the expected number of cases of malignant neoplasms and leukemia with fatal outcome may be 0.04 and 0.1 percent higher, respectively, than expected according to the "no threshold" hypothesis. The possible genetic sequelae in the first two generations of residents of these regions are estimated at hundredths of a percentage point in relation to the spontaneous levels [6].

Investigations have shown that there was accumulation of ^{90}Sr in the bones of residents of contaminated areas. In 1963-1980, strontium-90 levels in bones of expired adults of

Gomel Oblast constituted 1.23-1.95 strontium units (s.u.). According to the results of studies pursued in 1988-1989, 85 percent of those who died at the age of 16-90 years showed high ^{90}Sr levels in their bones (over 2 s.u.). Maximum strontium levels—5.8 s.u.—were found in the bones of those who expired at up to 30 years of age. It is not possible to relate accumulation of ^{90}Sr to the nature of illness that led to death. Studies are continuing.

According to a screening of victims of exposure to radiation, involving the use of SICH [HRC—human radiation counter] and SRP [research dosimeter] dosimetry revealed that about one percent of the subjects had elevated radionuclide levels in their body. Of this group, children constitute 0.9-3.7 percent in different regions and adolescents 12.3-20.4 percent; a significant part of the adults consists of pensioners (36-36.4 percent).

According to the findings of the institute, there are grounds to believe that adverse tendencies exist in BSSR with respect to the condition of the thyroid system of children and part of the adult population exposed to radionuclides (formation of risk groups for thyroid pathology, exacerbation of endemic goiter). There is some concern about the rise in the anemia syndrome among children in several rayons of this republic. For example, 38.7 percent of the children examined in 1989 in Cherikovskiy Rayon of Mogilev Oblast presented with the diagnosis of the anemic syndrome (versus 13.7 percent in 1985). Analogous data were obtained for Krasnopol'skiy Rayon in the same oblast. There is a tendency toward rise in incidence of the anemic syndrome in children of Slavgorodskiy Rayon in Mogilev Oblast.

These data were obtained as a result of implementation of universal dispensary supervision, use of ultrasound diagnostic equipment, the work of teams of physicians in the field, consultations with medical researchers, etc. They are indicative not only of the fact that morbidity exists, but also reflect improvement in picking up sick cases. Analysis of the effects of low doses of ionizing radiation combined with other deleterious factors (pesticides, nitrates, heavy metal ions, vitamin deficiency, etc.) in order to pinpoint the causes of diseases.

To assess the health status of inhabitants of monitored rayons in 1989 alone, 15 expeditions by institute staff were organized, and they examined about 10,000 people. In addition, extensive consultations were held in the monitored regions, as well as expert evaluation of morbidity, organization of work with HRC units and delivering talks for the public.

This institute became the organizational and methodological center in our republic on matters of radiation hygiene and radiation medicine. Republic-level and oblast seminars are held regularly on these questions. The First Scientific and Clinical Conference convened in December 1989, and it summed up the achievements of the institute over the preceding period. Since the institute was founded, its staff have published 11 methodological and instructive works (including 8 on the Union

level), 17 information bulletins, and 46 articles (4 abroad); 29 scientific papers were delivered.

The next task for the institute is to execute a set of assignments in the State Program for Eradication From BSSR of Consequences of the Accident at the Chernobyl AES: monitoring formation of dose loads, development of a set of sanitary and hygienic regulations to provide for radiation safety of the public, assessment of chronic combined effect of low doses of radiation, chemical and other factors on the health of residents of contaminated areas, development of a method of assessing the radiochemical sequelae in man and scientific validation of preventive treatment, rehabilitation, and dispensary observation of the public. Monitoring the condition of the thyroid system and specifics of formation of pathology in this system under the combined effect of radiation and strumogenic factors, development of methods for early detection, treatment and prevention of functional thyroid disturbances constitute a special task.

The results of investigations that are being pursued will have a medical and social impact; they will become the basis for scientific prognosis of man's vital functions as related to residing in different territories.

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UDC 616.441+616.441-006.5-036.21]:612.014.482
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Condition of Thyroid System and Distinctions in Formation of Thyroid Pathology in Belorussian Population Exposed to Iodine Radionuclides Due to Chernobyl Accident

907C0862C Minsk ZDRAVOOKHRANENIYE
BELORUSSII in Russian No 6, Jun 90 (manuscript
received 23 Mar 90) pp 11-16

[Article by L. N. Astakhova, Belorussian Scientific
Research Institute of Radiation Medicine]

[Text] The accident at the Chernobyl AES aggravated considerably the ecological situation in several parts of Belorussia. As a result of the accident, tens of millions of curies of radioactive substances were released into the environment. Among them, one should mention first of all the biologically significant isotopes of iodine, cesium and strontium. Considerable parts of BSSR, UkSSR, RSFSR (central economic region) and several parts of the globe were contaminated by radionuclides. About 70 percent of the most contaminated territory of the Soviet Union is in this republic [6].

As indicated by official publications [2, 17], radioactive fallout constituted 17×10^6 Ci ^{131}I , and 1.9×10^6 Ci ^{137}Cs . For the sake of comparison, during one of the most significant accidents at the nuclear installations in Windscale (Great Britain, 1957) fallout into the atmosphere constituted 20×10^3 Ci ^{131}I and 6×10^2 Ci ^{137}Cs [4, 11, 18]. The area of ^{131}I -contaminated ground was 518 km^2 . The estimated dose absorbed by the thyroid was 0.16 Gy (16 rad) in children who lived in the region of Windscale at the time of the accident and 0.095 Gy (9.5 rad) in adults.

In the "acute" period (first 2-3 months after the accident) iodine radionuclides were the main isotopes that had a radiation effect on the public, and already within the first few days they formed dose loads on the thyroid.

In this period, ^{131}I made the largest contribution to the radiation dose, and it was actively involved in the biological cycle (soil-plants-dairy cattle-man). A smaller role was played by external radiation exposure to all short-lived nuclides that fell out in the area, exposure due to inhalation of radioactive substances and exposure to the radioactive cloud [1, 2].

The total dose to the thyroid was formed primarily by partial contributions of ^{131}I , ^{132}I , ^{133}I incorporated in this organ, external gamma exposure and internal exposure to gamma-emitting cesium radionuclides.

The exceptionally high capacity of the thyroid gland to accumulate iodine radionuclides with a relative high dose rate created conditions for exposure of this organ in the inhabitants of regions of Belorussia that were subject to maximum contamination by iodine isotopes.

It was possible to lower appreciably the expected exposure dose in children by implementing protective measures: banning consumption of contaminated food (particularly milk), preventive iodine therapy, recommendations pertaining to behavior, as well as evacuation of inhabitants from areas subject to the greatest contamination. Thanks to these measures, it was possible to lower radiation exposure of the USSR population as a whole referable to incorporation of ^{131}I by an average of 50 percent, or 50,000 man-Sv (5 million man-rem) of the collective dose [2]. The efficacy of preventive measures was higher in large populated centers where there is centralized sale of foodstuffs.

In BSSR administration of stable iodine to the main population groups exposed to iodine radionuclides was started 3-5 days after the accident and later. It is known that stable iodine must be given 1-2 h before intake of isotopes for maximum (100 percent) protection of the thyroid. When it is given at the time of exposure protection constitutes 90 percent, and if this is done 6 h later, efficacy is only 50 percent [15, 18]. It must be borne in mind that because of the complex pattern of radioactive fallout over large territories in several BSSR rayons which were contaminated with iodine radionuclides, only partial or no preventive measures were carried out (for example, several rayons of Brest, Mogilev and even Gomel oblasts). As it was learned, most infants did not receive preventive iodine therapy.

In trying to prognosticate pathological states related to radiation exposure of the thyroid, one must bear in mind that the biological effect of radiation depends on many factors: radiation dose, dose rate, duration of exposure (physical indicators), age, sex, individual's genotype, initial condition of the thyroid and other biological variables.

Blastomogenic effects, which are in the category of stochastic effects, present a special hazard. Thyroid cancer can be induced even with a radiation dose of 1 Gy (100 rad). A statistically significant rise in incidence of thyroid tumors was also noted with lower doses [3, 9]. The latency period for development of cancer may last 10 to 25-30 years. It is shorter in children [5].

It is generally believed that the higher the dosage, the greater the effect. However, it was found that the relationship between number of cancer cases and dosage is not strictly linear. The incidence of radiogenic tumors rises with increase in dosage, reaches a peak, then drops [8, 18]. This phenomenon is attributed to destruction of

precarcinogenically altered cells. Conversely, the risk of developing hypothyroidism rises with high doses.

In people who survived the atomic bombing in Japan and explosion of the hydrogen bomb on the Marshall Islands, the main forms of thyroid pathology were cancer, hyperplastic (adenomatous) nodes and hypothyroidism, which were detected after 10-30 years [7, 8, 16]. Nodes and hyperthyroidism were encountered many times more often than cancer of the thyroid gland. Thyroid hypofunction developed in the presence of hyperplastic nodes much more often in women and individuals exposed to radiation at up to 10 years of age. Aside from the above forms of pathology, adenoma and thyroiditis cases were also found.

There was a higher incidence of thyroid hypofunction on Rongelap Island, where the inhabitants were exposed to high doses of radiation (over 10 Gy) in 1954, mainly due to short-lived iodine radionuclides [7, 8, 16]. Atrophy of the gland with clinical hypothyroidism was diagnosed in 2 boys (3 percent). Nineteen percent of the inhabitants developed subclinical hypothyroidism, in spite of thyroxine therapy administered since 1965. A high incidence (61 percent) of subclinical hypothyroidism was found in patients operated for thyroid nodes. It is believed that insufficiency of the thyroid could have developed in all residents of Rongelap if preventive thyroxine therapy had not been started in 1965. In residents of Utiirik Island, where the mean absorbed dose was lower by a factor of 10 [12, 13], the incidence of laboratory-diagnosed hypothyroidism was lower, and for this reason universal preventive thyroxine therapy was not instituted.

It is generally conceded that radiation-induced hypothyroidism can develop both at the early stages after radiation exposure and many years later. The pathogenesis of "early" hypothyroidism, which developed with high radiation doses, is based primarily on degeneration and fibrosis of interfollicular stromal vessels and then the follicular epithelium [3]. With exposure to low radiation doses, the direct effect on epithelial cells is examined, since this leads to development of hypothyroidism in the long term, the beginning of which depends not only on physical, but also biological factors: age, sex, genotype of the victim, initial status of the gland, iodine content of foodstuffs, etc. Autoimmune thyroiditis holds an important place in the pathogenesis of "delayed" hypothyroidism.

In assessing radiation effects on the thyroid of children, one must bear in mind the higher radiosensitivity of the child's gland, as compared to adults, the greater capacity of a growing organ to accumulate radioiodine per gram tissue due to the higher metabolic rate, rate of proliferative processes and hormonal activity of this gland. When there is a change in a child's hormonal status, the triggering element of which is radiation damage to the thyroid, there is a greater risk of pluriglandular dysfunction, disharmonious development of children and adolescents. As a result of secondary neuroendocrine disintegration, it is possible for a rise in the future in

incidence of tumors of other endocrine glands: adenoma of the pituitary, adrenal cortex, insuloma, cancer of the pancreas, seminoma, breast cancer, and cystadenomatous changes in the ovaries.

Endemic goiter, which is inherent in some regions of Belorussia that were subject to radionuclide contamination is a factor that aggravates radiation effects in the thyroid of BSSR residents. Endemic goiter is a multifactorial disease based on an inherited predisposition (enzyme system deficiency) combined with environmental factors: geochemical, dietary, sociohygienic and technogenic. A shortage of iodine in the environment is one of the chief causes of endemic goiter in BSSR. The decline in iodine content of soil, air and drinking water leads to shortage thereof in food and, as a result, less uptake of iodine in the thyroid, followed by functional and structural changes in this organ. Low levels of a number of trace elements (copper, cobalt), high levels of manganese and humins are inherent in BSSR, particularly regions of Polesye, and with the iodine shortage this creates conditions that accelerate development of endemic goiter.

In the 1930's-1940's, Ye. A. Korchits and A. A. Greyman found that about 35 percent of the individuals in different rayons of Gomel Oblast had endemic grade I-II enlargement of the thyroid and 3-10 percent had goiter. The preventive measures that were instituted improved somewhat the endemic situation in the republic. In the period from 1970 to 1975, the incidence of goiter dropped each year. From 1975 to 1985 there was relative stabilization of this indicator (mean for BSSR 22.2/100,000 population by 1985, 22.7/100,000 in Gomel Oblast and 22.9 in Mogilev Oblast). In spite of the fact that the problem of endemic goiter in the BSSR did not lose its importance in this period, attention to regular and specific prevention of the endemic diminished, and several years prior to the Chernobyl accident preventive group iodine therapy was discontinued.

The intensification of adverse radiation effects on the thyroid in endemic areas can be manifested in different ways. When there is a low iodine content in the diet, higher incorporated doses are formed, and radioiodine is excreted from the thyroid more slowly. In endemic areas, conditions develop that favor intensification of proliferative processes and, consequently, faster development of neoplasms of the thyroid gland. On the other hand, an attempt to suppress the effects of proliferation with iodine preparations can be instrumental in development of functional insufficiency. This circumstance complicates considerably the implementation of preventive measures. In endemic regions, there is also a greater danger of development of autoimmune processes in the thyroid, which aggravate both functional insufficiency and proliferative processes in response to additional aggressive factors.

In recent years, there has been increasing discussion in the literature of the question of adverse effects on the thyroid system of long-term preventive iodine therapy

[10, 14, 18]. In regions that are endemic for goiter where iodine is given preventively, there has been a rise in incidence of autoimmune thyroiditis, goiter and papillary cancer of the thyroid.

It must be noted that unwise and prolonged intake of stable iodine after the Chernobyl accident could also have made some contribution to development of deviations in the thyroid system of children. It is known that administration of nonradioactive iodine is warranted as a short-term measure. Due to the fact that some medical personnel are not adequately informed, preventive iodine therapy instituted in early May 1986 for children relocated from Gomel Oblast was continued for the entire month of May and, in some health-care institutions, in June 1986 as well. It is known that administration of nonradioactive iodine to children and pregnant women should not be continued without appropriate indications due to the possibility of side reactions, including development of goiter, hypothyroidism, thyrotoxicosis, thyroiditis and allergic reactions [18].

The difficulty of the situation that developed in BSSR in connection with the accident at the Chernobyl AES lies in the fact that thousands of children living in southern regions of BSSR (Gomel, Brest and Mogilev oblasts) at the time of the accident were exposed to iodine radionuclides, and the radiation doses to their thyroid are being determined at the present time. According to the preliminary data of the Scientific Research Institute of Biophysics, USSR Ministry of Health, absorbed doses are considerably higher in residents of the 30-km zone and several populated centers of Khoynikskiy and Braginskiy rayons that are not included in this zone. Infants and preschool (at the time of the accident) children were stricken the most with respect to dose loads. Consequently, medical workers should be particularly anxious about the physical status of children in these age groups.

Analysis of data from a screening of the child population, which was started in 1986 by the staff of the Minsk Medical Institute (Second Department of Childhood Diseases, Problem Laboratory of Childhood Pathology of the Central Research Laboratory) and continued since 1989 by the staff of the Belorussian Scientific Research Institute of Radiation Medicine (laboratory of neurohumoral homeostasis) and visiting teams of endocrinologists from endocrinological dispensaries of this republic, indicates that there is a generally high incidence of changes in the thyroid of children in all groups examined, including control areas (Braslavskiy Rayon of Vitebsk Oblast, Minskiy Rayon, city of Minsk).

The most important problem is to diagnose preclinical stages of thyroid pathology under conditions of combined effects of low doses of radiation and strumogenic factors. Endemic grade I-II enlargement of the thyroid should become the object of close attention of physicians, since it is an additional risk factor for development of pathological processes in this organ.

As a result of dynamic observation of the child population in 1986-1989, it can be stated that, in these years, there has been a general trend toward exacerbation of endemic goiter in most of the monitored rayons.

A screening of children in Braginskiy, Khoynikskiy and Narovlyanskiy rayons in 1986 (according to findings of scientific expeditions) revealed 41.8 percent with grade I-II enlargement of the thyroid. In 1987, this figure rose to 57.1 percent. By the end of 1989, the incidence of grade I-II hyperplasia in children of different populated centers in Khoynikskiy Rayon ranged from 50.2 to 70.8 percent.

In 1989 in Braginskiy Rayon, the incidence of grade I-II hyperplasia of the thyroid dropped to the 1986 level (41.3 percent), which was attributable, to some extent, to improved diet (iodine and vitamin supplements in foods), therapeutic and preventive measures. Analysis of individual dynamics in this rayon revealed a reduction in size of the thyroid in 38.5 percent of the children and enlargement in 15 percent. The positive direction of changes in incidence of hyperplasia of the thyroid gland did not affect the youngest age groups at all. In 3-year-old children, grade I enlargement of the thyroid was diagnosed in 22.9 percent, grade II in 4.2 percent of those examined (there was not a single case of grade II hyperplasia in children of this age group in control regions).

The rise in number of children in Braginskiy, Khoynikskiy, Narovlyanskiy, Vetkovskiy, Cherikovskiy and other rayons at risk for hypothyroidism and autoimmune diseases of the thyroid merits serious attention. In 1989, signs of hypothyroidism (elevation of TSH [thyrotropic hormone] level of $+2\delta$ in relation to the control) were recorded reliably more often among children exposed to iodine radionuclides in the prenatal, postnatal periods and infancy than in other age groups (findings of scientific expedition to Cherikovskiy Rayon).

The results of an in-depth examination of children with grade I-II enlargement of thyroid at the clinic of the Belorussian Scientific Research Institute of Radiation Medicine in 1989 revealed that there were hormonal deviations in 55.1 percent. The most typical findings were elevation ($+2\delta$ in relation to control) of TSH level, T_3 (free fraction) and TBG (thyroxine-binding globulin), as well as increased titer of antibodies to thyroglobulin, titer of microsomal antibodies (endocrinology laboratory of the Belorussian Scientific Research Institute of Radiation Medicine, BSSR Ministry of Health).

Signs of activation of the B system of immunity (high B-lymphocyte and immunoglobulin G levels), and a tendency toward decrease in number of suppressor T lymphocytes (laboratory of clinical immunology, Belorussian Scientific Research Institute of Radiation Medicine) were established in the immune status of children.

According to data of the clinic of the Belorussian Scientific Research Institute of Radiation Medicine, (BSSR Ministry of Health) in 10 months a total of 739 children

with endocrinological pathology had been seen there, including 83 (11 percent) with autoimmune thyroiditis, 2 (0.3 percent) with subacute thyroiditis and 46 children (6 percent) with grade I-II hyperplasia of the thyroid and manifestations of autoimmunization.

Ultrasound examination of children with the tentative diagnosis of thyroid hyperplasia revealed various acoustic phenomena in 23 percent, reflecting some type of thyroid pathology: nodular elements, signs of infiltrative-inflammatory and fibrous-sclerotic changes, stronger vascularization with dilatation of vessels (endocrinology laboratory of the Belorussian Scientific Research Institute of Radiation Medicine).

According to the data of the republic endocrinological dispensary, from 1985 to 1988 the incidence of goiter rose everywhere in BSSR (from 31.2 to 39.7 cases per 100,000 in Brest Oblast, from 21.4 to 30.1 in Grodno Oblast, from 20.1 to 43.2 in Minsk Oblast, from 22.7 to 39.8 in Gomel Oblast, from 21.9 to 33.0 in Mogilev Oblast, and from 22.3 to 31.4/100,000 in BSSR as a whole. In 1989, the incidence of goiter in Gomel Oblast was already 53.8 per 100,000 and in Mogilev Oblast 43.8. We are alerted by the fact that there was a rise in thyrotoxicosis in adult residents of Gomel Oblast. In the period from 1985 to 1988, thyrotoxicosis increased there from 9.2 to 23.9 cases per 100,000 (in the same period it rose from 1.65 to 3.3 in Mogilev Oblast and from 7.4 to 11.5/100,000 in BSSR as a whole).

Thus, there are grounds to believe that adverse trends have developed in BSSR with respect to status of the thyroid system in children and part of the adult population exposed to radionuclides: formation of risk groups for hypothyroidism and autoimmune diseases of the thyroid, increased incidence of autoimmune thyroiditis in the presence of exacerbation of endemic goiter.

The area-wide rise in incidence of goiter in BSSR in recent years can be attributed to the increased attention given to thyroid pathology, improved diagnosis, absence of regular iodine treatment to prevent endemics, as well as the cumulative effect of the poorer ecological situation in this republic (technogenic and chemical pollution of the environment, consequences of intensive water improvement work) and adverse social, psychological and alimentary (unbalanced diet) factors.

One should consider the additive effects of both radiation and strumogenic factors among the causes of the negative trends demonstrable in 1986-1989 in the status of the thyroid system of Belorussian children. It must be borne in mind that the autoimmune and blastomogenic effects on the immune system of growing children can be significantly intensified due to the adverse effects of intensive environmental pollution of the environment by xenobiotics, many of which are immunotoxins, and low doses of radiation exposure of those who live permanently in the monitored regions. One must anticipate and be prepared for the resonance effect of adverse factors. For this reason, special attention must be given

to radical improvement of the ecological situation in this republic and solving the problem of relocating the residents of populated centers exposed to significant contamination by iodine radionuclides who continue to live in monitored areas.

In the existing situation, medical workers must give priority to the search for and formation of groups at risk for autoimmune disease, neoplasms of the thyroid, hypothyroidism, functional insufficiency of other organs and systems and implementing primary preventive care. At this stage, in the matter of monitoring health status and condition of the thyroid system of individuals exposed iodine radionuclides priority should be given to children up to 6 years of age (at the time of the accident), adolescents and children with health problems in whom the thyroid incorporated 200 or more rad, those with endemic enlargement of the thyroid, as well as individuals involved in the cleanup at the Chernobyl AES during the first 2-3 months after the accident. Children relocated from the 30-km zone, many of whom received dose loads to the thyroid in excess of 5 Gy merit special attention.

It is equally important to establish a special "iodine" register on the republic level of individuals exposed to radiation and to map rayons in Gomel, Mogilev and Brest oblasts according to severity of "iodine endemic," with involvement of the Belorussian Scientific Research Institute of Radiation Medicine, scientific research institutes of the Belorussian Academy of Sciences, oblast and rayon sanitary and epidemiological stations, endocrinological dispensaries, and oblast centers for radiation medicine. Success in preventing medical sequelae of the Chernobyl accident will depend largely on involvement of everyone in solving this problem.

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UDC 612.014.482-053.2/6:362.147

Distinctions in Dispensary Care of Children Exposed to Radiation as a Result of the Accident at the Chernobyl Nuclear Power Plant

907C0862D Minsk ZDRAVOOKHRANENIYE BELORUSSII in Russian No 6, Jun 90 (manuscript received 20 Feb 90) pp 21-23

[Article by L. A. Sivolobova, L. M. Vasilevich, and A. I. Korkhov, Dispensary-Polyclinic Department of Clinic of the Belorussian Scientific Research Institute of Radiation Medicine]

[Text] The requirements for dispensary care of the inhabitants from regions of radionuclide contamination have increased because of the Chernobyl accident. Children are particularly sensitive to radiation, so that medical workers were faced with the extremely important task of carrying out the full set of measures aimed at preserving and strengthening the health of children, lowering morbidity, preventing development of diseases, primarily those related to radiation exposure.

Dispensary care of children exposed to radiation acquired the name of special dispensary care. Special dispensary care does not mean that there is something new in a physician's work, rather it refers to the routine meticulous work of the polyclinic physician and his assistant, the nurse.

Dispensary care of children who were affected by the accident at the Chernobyl AES [nuclear power plant] began with making a record of the child population. Considering the migration process in 1986-1987 of the residents of Gomel Oblast, this phase of the work required considerable time and effort on the part of local health care agencies.

There must be a personal record of all children exposed to ionizing radiation, who lived in the monitored regions and had moved to other populated centers in this republic or elsewhere.

The "Dispensary care card," F-No 131/U-86 is used to keep a record of the child population, as well as to check appropriateness of periodic examinations. It is filled out on the basis of rosters compiled by the medical personnel of FAP [feldsher-obstetric centers], walk-in facilities, polyclinics or polyclinic departments.

The obtained information is checked against the data in the ZhES [expansion unknown], rural soviets, OVD [internal affairs department] and, then are verified twice a year. FAP's, district and numbered hospitals transmit

The table illustrates the system of special dispensary observation of children who were victims of the Chernobyl accident. The plus sign refers to frequency of examination (screening). Children are examined by a pediatrician at specified times.

[illegible]

System of monitoring children and adolescents placed on dispensary rolls in connection with radiation exposure as a result of Chernobyl accident (Continued)

Examination by physicians and tests	Age of children										
	first year	2 years	3 years	4 years	5 years	prior to school enrollment	1st and 2d grades	3d grade	4th, 5th and 7th grades	6th grade	8th grade
—category II	++	++	++	++	++	++	++	++	++	++	++
—category III	+					+					+
—category IV	+					+					+
—category V	+					+					+
Endocrinologist											
—category II	++	++	++	++	++	++	++	++	++	++	++
—category III	++	++	++	++	+	+	+	+	+	+	+
—category IV	+	+	+	+	+	+	+	+	+	+	+
—category V*											
TSH, T ₃ , T ₄											
—category II	+	+	+	+	+	+	+	+	+	+	+
—category III	+	+	+	+	+	+	+	+	+	+	+
—category IV	+	+	+								
Blood	+	+	+	+	+	+	+	+	+	+	+
Urine	+	+	+	+	+	+	+	+	+	+	+
Stool for helminth eggs	+	+	+	+	+	+	+	+	+	+	+

*In regions endemic for goiter.

Organization of comprehensive preventive examinations is the most important element of dispensary care of the child population.

Preventive examinations are a labor-consuming process. Medical workers spend most of their time on anthropometric measurements, testing vision and hearing, the cardiovascular system, musculoskeletal system, taking blood pressure and keeping medical records.

Organization of laboratory tests is an important problem in dispensary care. The district nurse must give referrals in advance for laboratory tests on children in the district she services so that on the day they are examined by a pediatrician and other specialized physicians the test results would already be entered in the children's chart.

The optimum variant is to form and organize combined visiting teams consisting of specialist physicians, laboratory technician and nurse for functional tests.

It is suggested that health care agencies organize team of specialists from republic, kray and oblast hospitals, medical VUZ's and scientific research institutes, as well as from municipal health care institutions for dispensary screening of the adult and child population of rural regions with a shortage of physicians (Gomel and Mogilev oblasts).

When the medical teams arrive for dispensary examination of monitored rayons of Gomel and Mogilev oblasts

exposed to radiation due to the Chernobyl accident, the TsRB administration specifies where they are to work and sees that children are sent there. There is a unified plan to determine which group of children is to be examined and when. The results of the examination and screening are entered in the outpatient charts, which are collected in advance by the TsRB medical personnel.

Monitoring category II children referred to the 3d-5th health groups who require frequent dispensary observation (more than 3 times a year) are examined twice a year in the dispensary department of the Belorussian Scientific Research Institute of Radiation Medicine, while other check-ups are carried out by the TsRB and oblast hospital. It is very important not to forget the principle of continuity: the examination results and recommendations about preventive therapy at the TsRB for such a child, who has undergone dispensary examination at a republic-level specialized institution, are sent to the TsRB, while information about dispensary observation carried out by the TsRB and health status of the child in the elapsed period are transmitted when the child is next referred for an in-depth examination at a republic-level institution.

The second form of dispensary screening is organized referral of children from monitored rayons to the dispensary department of the clinic of the Belorussian Scientific Research Institute of Radiation Medicine in accordance with a schedule prepared in advance at the start of

the year and coordinated with oblast health departments. In addition, there is the extensive practice of individual call-ups [for examination] that are mailed to the child's home.

The third form of dispensary observation is to hospitalize dispensary patients in highly qualified hospitals: oblast hospital, clinic of the Belorussian Scientific Research Institute of Radiation Medicine and other republic-level pediatric facilities. The results of diagnostic laboratory tests and recommendations for treatment are entered in the discharge chart. An excerpt from the case history is sent to the outpatient-polyclinic institution in the district of the patient's residence, and it is taken into consideration when carrying out dispensary care.

Organization of health education work is a rather important element in the system of disease prevention and, in particular, prevention of possible complications related to ionizing radiation exposure. Every physician, feldsher and nurse must work on development of healthy children, their hygienic education, organization of schedule, diet, conditioning, physical education, and the need for regular preventive examinations and following physicians' recommendations.

The work of all scientific research medical institutes and departments of pediatrics in this republic must be directed first and foremost toward solving problems of health care practices for prevention and treatment of diseases related to radiation exposure as a result of the accident at the Chernobyl AES.

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UDC 614.73:612.1-053.2:577.1(476.2)(476.4)

Changes in Some Biochemical Parameters of Blood in Children Residing in Radionuclide-Contaminated Areas

907C0862E Minsk ZDRAVOOKHRANENIYE
BELORUSSII in Russian No 6, Jun 90 (manuscript
received 14 Feb 90) pp 29-32

[Article by S. V. Petrenko, V. A. Zaytsev, R. A. Dudinskaya, T. N. Petrovskaya, and A. I. Nemets¹, Belorussian Scientific Research Institute of Radiation Medicine]

[Text] It is already over three years that the inhabitants of several rayons of Gomel and Mogilev oblasts have been living in areas contaminated with radionuclides of a broad chemical spectrum. According to the findings of epidemiological studies, there is a trend toward rise in a number of diseases, such as anemia, functional disturbances of the thyroid, autonomic vascular dystonia and a few others.

To date the question of correlation between the above diseases in children, amount of incorporated ^{137}Cs and density of its contamination of the area has not been explored, although expressly this radionuclide makes the main contribution to the dose load on the body [1].

Our purpose here was to investigate the different clinico-biochemical parameters and hormone levels in the blood of children in Checherskiy Rayon of Gomel Oblast and Krasnopol'skiy Rayon of Mogilev Oblast.

Material and Methods

A total of 140 children ranging in age from 5 to 15 years were examined in April 1989 with consideration of density of ^{137}Cs contamination of the area of their residence. Populated centers were arbitrarily divided into the following zones: first—with contamination density above 60 Ci/km², second—40-60 Ci/km², third—20-40 Ci/km², fourth—5-20 Ci/km², and fifth—less than 5 Ci/km². The last zone was used as the reference. Two groups were singled out in the fourth zone which consisted of children with incorporated cesium-137 levels of more and less than 1 μCi . In the rest of the zones, we gathered statistics on children with less than 1 μCi incorporation per child.

Complete analysis of peripheral blood was made on all of the children examined. Hormone levels of the thyroid and serum thyrotropin in blood samples to which 4 percent EDTA solution was added, were assayed using the radioimmune sets of the Abbott Company (USA). Ferritin and beta-2-microglobulin levels were analyzed using the reagent kits produced by the Institute of Bioorganic Chemistry, Belorussian Academy of Sciences. Na⁺, K⁺-ATPase activity was tested in red cell membranes [6, 3]. An HRC [human radiation counter] was used to measure ^{137}Cs levels.

Results and Discussion

In analyzing our results (Tables 1 and 2), we failed to find a direct relationship between radiocesium in the children and its amount on soil. Thus, we found less accretion of ^{137}Cs in children in zones with high contamination density (1st zone—Krasnopol'skiy Rayon and 3rd zone—Checherskiy Rayon) than in those living in cleaner areas.

Table 1. Clinicobiochemical parameters and composition of peripheral blood in children of Krasnopol'skiy Rayon, Mogilev Oblast

Density of contamination	Over 60 Ci/km ²		40-60 Ci/km ²		5-20 Ci/km ²		Less than 5 Ci/km ²	
	zone 1		zone 2		zone 4		zone 5	
	number of cases	blood parameters	number of cases	blood parameters	number of cases	blood parameters	number of cases	blood parameters
Erythrocytes, 10 ¹² /l	15	3.48+/-0.12	9	3.35+/-0.25	7	3.57+/-0.14	8	3.45+/-0.12
Hemoglobin, g/l	19	120.00+/-2.80	9	124.00+/-2.20	7	125.00+/-3.10	8	119.00+/-3.70
Thrombocytes, 10 ⁹ /l	14	250.00+/-15.00	9	185.00+/-3.50	7	244.00+/-19.00	8	251.00+/-20.00
								p _{2,4} <0.01
Lymphocytes, percent	19	42.00+/-2.80	9	39.00+/-6.10	7	53.00+/-6.30	8	36.00+/-3.90
								p _{3,4} <0.05
Leukocytes, 10 ⁹ /l	19	6.20+/-0.47	9	6.30+/-0.72	7	6.20+/-0.60	8	7.20+/-0.67
Triiodothyronine, nmol/l	16	2.44+/-0.12	15	2.69+/-0.15	6	2.97+/-0.32	14	2.52+/-0.12
Thyroxine, nmol/l	17	110.50+/-5.50	15	106.20+/-4.70	7	125.40+/-11.6	14	109.30+/-5.80
Thyrotropin, µU/ml	17	2.58+/-0.49	15	3.08+/-0.65	6	6.48+/-1.48	14	3.15+/-0.50
		p _{1,3} <0.025		p _{3,4} <0.05				p _{3,4} <0.05
Na ⁺ , K ⁺ -ATPase, µmol Pi/h/mg protein	20	0.130+/-0.017	12	0.164+/-0.013	7	0.187+/-0.037	12	0.099+/-0.012
				p _{2,4} <0.01				p _{3,4} <0.05
Ferritin, ng/ml	7	28.90+/-3.5	9	32.70+/-4.70	5	52.80+/-8.60	14	34.90+/-5.10
		p _{1,3} <0.05		p _{2,3} =0.05				
Beta-2-microglobulin, mg/l	19	0.65+/-0.10	11	0.91+/-0.13	7	1.11+/-0.13	20	1.70+/-0.18
		p _{1,4} <0.001		p _{2,4} <0.001		p _{1,3} <0.01		p _{3,4} <0.025
Incorporated ¹³⁷ Cs, µCi	22	0.17+/-0.02	16	0.23+/-0.02		—		—
				p _{1,2} <0.05				

Table 2. Clinicobiochemical parameters and composition of peripheral blood in children of Checherskiy Rayon, Gomel Oblast

Density of contamination	20-40 Ci/km ² (3d zone)		5-20 Ci/km ² (4th zone)				Less than 5 Ci/km ² (5th zone)	
			under 1 µCi		over 1 µCi			
	number of cases	blood parameters	number of cases	blood parameters	number of cases	blood parameters	number of cases	blood parameters
Erythrocytes, 10 ¹² /l	10	4.20+/-0.07	21	3.90+/-0.08	15	4.30+/-0.10	7	4.20+/-0.12
Hemoglobin, g/l	10	129.00+/-1.80	21	123.00+/-1.90	15	131.00+/-3.30	7	127.00+/-5.80
Thrombocytes, 10 ⁹ /l	10	238.00+/-12.00	20	203.00+/-9.20	15	220.00+/-9.30	7	198.00+/-10.80
Lymphocytes, percent	10	35.00+/-2.60	21	33.00+/-2.40	15	34.00+/-1.70	7	26.00+/-1.90
								p _{1,4} <0.05
Leukocytes, 10 ⁹ /l	10	5.90+/-0.57	21	7.20+/-0.48	15	5.70+/-0.36	7	5.20+/-0.49

Table 2. Clinicobiochemical parameters and composition of peripheral blood in children of Checherskiy Rayon, Gomel Oblast (Continued)

Density of contamination	20-40 Ci/km ² (3d zone)		5-20 Ci/km ² (4th zone)				Less than 5 Ci/km ² (5th zone)	
	number of cases	blood parameters	under 1 µCi		over 1 µCi		number of cases	blood parameters
			number of cases	blood parameters	number of cases	blood parameters		
						p _{2,3} <0.025		p _{2,4} <0.01
Triiodothyronine, nmol/l	9	2.40+/-0.12	27	2.61+/-0.09	15	2.37+/-0.17	7	2.54+/-0.26
Thyroxine, nmol/l	6	114.70+/-10.60	27	96.00+/-5.20	15	75.90+/-5.20	7	81.90+/-3.50
		p _{1,3} <0.01				p _{2,3} <0.01		p _{1,4} <0.025
Thyrotropin, µU/ml	10	2.40+/-0.48	25	2.38+/-0.25	15	2.00+/-0.45	6	1.38+/-0.21
Na ⁺ , K ⁺ -ATPase, µmol Pi/h/mg protein		p _{1,2} <0.025						
Ferritin, ng/ml	9	25.90+/-3.34	27	48.00+/-6.48	15	57.20+/-8.98	7	61.30+/-9.58
				p _{1,2} <0.01		p _{1,3} <0.01		p _{1,4} <0.01
Beta-2-microglobulin, mg/l	10	1.82+/-0.15	28	1.60+/-0.14	15	1.45+/-0.10	7	1.50+/-0.17
						p _{1,3} =0.05		
Incorporated ¹³⁷ Cs, µCi	10	0.065+/-0.005	24	0.11+/-0.04	15	2.33+/-0.55	7	0.63+/-0.04
		p _{1,4} <0.01		p _{2,4} <0.01		p _{2,3} <0.01		p _{3,4} <0.01

With reference to composition of peripheral blood of the children examined, it can be stated that no anemia was demonstrable in the groups of children tested, although mean red cell count was somewhat lower in Krasnopol'skiy Rayon than in Checherskiy Rayon. There was an insignificant tendency toward leukopenia in children of Checherskiy Rayon living in the 4th zone when they accreted more than 1 µCi ¹³⁷Cs (mean 2.33+/-0.55 µCi). Some lymphocytosis was demonstrated in children from Krasnopol'skiy Rayon living in the fourth zone, as compared to lymphocyte count in the blood of children from the cleaner fifth zone. The changes in levels of other formed blood elements as related to density of radioactive cesium contamination of the territory were statistically unreliable.

Examination of the hormonal status of the thyroid revealed that the concentration of total thyroxine in blood was higher (by 29 percent) in children of Checherskiy Rayon living in strictly monitored zones (radiocesium contamination density in excess of 15 Ci/km²—third zone) than in the reference zone; however, this elevation (to 115 nmol/liter) was within the physiological range. At the same time, children from the fourth zone with over 1 µCi incorporated ¹³⁷Cs have lower (by 21 percent) thyroxine levels than children living in the same zone but with less incorporation of the radionuclide. We failed to demonstrate differences in serum thyroxine levels in children from different zones of Krasnopol'skiy Rayon.

We found no relationship between residence zone and level of ¹³⁷Cs uptake and concentration of blood triiodothyronine in each of the rayons.

There is a tendency toward elevation of thyrotropin in blood of children living in strictly monitored zones (third zone) of Checherskiy Rayon, as compared to the fifth zone. However, this trend is statistically mild. In Krasnopol'skiy Rayon, we observed elevation (two-fold) of thyrotropin level in children from the fourth zone where there is insignificant radiocesium contamination, as compared to the fifth, reference zone. At the same time, thyrotropin level was low (down to 1/2-1/5th) in the first and second zones with high contamination density, as compared to the same fourth zone.

Examination of activity of Na⁺, K⁺-dependent ATPase in red cell membranes of residents of Checherskiy Rayon, revealed a decline (by 40 percent) in enzyme activity in children from the third strictly monitored zone. In Krasnopol'skiy Rayon, enzyme activity was highest in the fourth zone where contamination is insignificant; it was lower in the first and second more contaminated zones, but higher (by 30 and 66 percent) than in the reference, fifth zone.

In order to evaluate iron supply [5], we assayed serum ferritin (high-molecular protein) which serves as a molecular reservoir for nonhemic iron in tissues. Similar findings were made in children of both rayons: ferritin concentration was highest in the reference zone and the

fourth zone with minimal contamination, and its levels decreased as density of ^{137}Cs contamination increased in the place of residence (1st, 2d and 3d zones) to 5/8-1/2 of the level in the reference zone.

We assayed blood levels of low-molecular protein beta-2-microglobulin for preclinical detection of renal insufficiency of diverse genesis, some immune diseases (rheumatoid arthritis, lupus) and possible effects of radiocesium on the kidneys. Beta-2-microglobulin level was the same in children residing in the reference zone and the zone of insignificant contamination (5th and 4th) of Checherskiy Rayon, whereas in the strictly monitored zone (3d) it was 25 percent higher. Serum findings were different for children from Krasnopol'skiy Rayon, where the highest concentration of this protein was demonstrated in the fifth, reference zone. With increase in density of ^{137}Cs contamination, the concentration of beta-2-microglobulin decreased: by 35 percent in the fourth zone, 46 and 62 percent respectively in the second and first zones.

With reference to the above data, it should be noted that the fact that there is some instability to blood elements (leukopenia, lymphocytosis) in children from contaminated regions does not constitute grounds for alarm. Repeated monitoring and comparison to analogous results of prior tests are needed for a definitive assessment [4]. The increase in thyrotropin concentration along with elevation of thyroxine levels (Checherskiy Rayon) in the blood of children from ^{137}Cs -contaminated rayons should alert us with respect to transient forms of hypothyroidism. Hypothyroid states reduce the intensity of protein synthesis in the body as a whole. Activation of Na^+ , K^+ -dependent ATPase could also be one of the compensatory mechanisms aimed at inhibition of protein-synthesizing processes [2], and an excess of the latter could destabilize the effects of low doses of ionizing radiation on the structure of nucleic acids.

The decrease in concentration of serum ferritin in children from the strictly monitored zones suggests the presence of relative iron-deficiency states.

There was dissimilar change in levels of beta-2-microglobulin as related to rayon and zones, and this is perhaps related to differences in immunological status of children from these rayons.

On the whole, it can be concluded from the clinicobiochemical parameters analyzed that we failed to demonstrate a clear-cut relationship between density of ^{137}Cs contamination of place of residence, or its amount incorporated in the body, and the selected parameters. At the same time, there are some changes both on the level of the regulatory elements of the body (pituitary, thyroid) and metabolic processes (involving Na^+ , K^+ -ATPase and functionally important blood proteins (ferritin, beta-2-microglobulin). It should be assumed that there is a multifactor effect (chemical, radiation, psychogenic) that worsens the condition of children residing in areas that were affected by the accident at the Chernobyl AES.

Footnotes

1. These authors wish to express their appreciation to chief physicians P. B. Boyarchik of the Checherskiy Central Rayon Hospital and V. K. Penkovsky of the Krasnopol'skiy Central Rayon Hospital for their cooperation in preparing this article.

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UDC 612.89+612.45]-053.2-02:614.73

Status of Adrenosympathetic System of Children Residing in Areas Differing in Density of Radiation Contamination

907C0862F Minsk ZDRAVOOKHRANENIYE
BELORUSSII in Russian No 6, Jun 90 (manuscript
received 14 Feb 90) pp 32-33

[Article by V. G. Balakleyevskaya, I. N. Nekko, and S. V. Petrenko, Minsk]

[Text] Incorporation of radionuclides, including radiocesium, as well as exposure to total body radiation are apparently powerful factors affecting regulatory and biochemical processes in individuals residing in contaminated areas. However, there has been insufficient investigation of the nature of effects of combined internal and chronic external radiation in low doses on the adrenosympathetic system (ASS) and early stages of adaptation of the human body.

Our objective was to analyze catecholamine metabolism in children with different levels of radiocesium accretion, who reside in areas differing in density of radiation contamination.

ASS was evaluated in children with different levels of accreted radiocesium according to excretion in morning urine of epinephrine (E), norepinephrine (NE), dopamine (DA) by a fluorimetric method [2], and basic metabolites of catecholamines: homovanillic (HVA) and vanillylmandelic (VMA) acids by thin-layer chromatography on Silufol plates [1].

A study was made of 62 children 12-15 years of age, of both sexes, residing in areas with contamination density ranging from 5 to 15 Ci/km² (1st group) and from 15 to

40 Ci/km² (2d group). In addition, the above parameters were analyzed in these child groups as a function of level of accretion of radiocesium (measured with the HRC unit [human radiation counter]).

Each group of children was divided into 2 subgroups: in one of them radiocesium accretion was less than 1 µCi and in the other it was more than 1 µCi.

The children were classified in the second health group without any marked functional disturbances.

In the first group, we demonstrated an increase in excretion of epinephrine and a tendency toward increased excretion of catecholamine (CA) metabolites in children with higher levels of radiocesium accretion (Table).

Indicators of excretion in urine of catecholamines and their metabolites (ng/mg) in children of Gomel Oblast residing in areas differing in contamination density, as a function of accretion of radiocesium

Indicators	1st group, 5-15 Ci/km ²		2d group, 15-40 Ci/km ²	
	>1.0 µCi	<1 µCi	>1.0 µCi	<1 µCi
Epinephrine	17.87±0.85*	13.25±1.24	17.53±1.24	19.15±1.77
Norepinephrine	10.83±0.67	13.13±1.24	11.03±0.48	12.59±0.59
Dopamine	164.70±12.42	174.75±18.63	264.80±10.39*	309.25±13.45
Homovanillic acid	4430.00±240.00	3860.00±280.00	4330.00±310.00	3900.00±270.00
Vanillylmandelic acid	6060.00±590.00	4910.00±400.00	6120.00±340.00*	4610.00±280.00
Total catecholamine excretion	10683.40±843.90	8971.10±701.10	10742.60±662.10*	8850.90±565.80

Footnote: *p<0.05 in relation to subgroup of children with lower level of radiocesium accretion.

In the second group of such children, there was even greater increase in VMA excretion, but decreased excretion of dopamine, with no change in other parameters. Considerably higher levels of dopamine excretion were demonstrated in children residing in areas with high contamination density, and increased epinephrine excretion in the subgroup with lower levels of radiocesium accretion.

Excretion levels of VMA and total excretion of the main CA metabolites were higher in children with greater accretion of radiocesium, and this was particularly marked in the second group.

These data are indicative of activation of CA metabolism in children with greater incorporation of radionuclides.

We were impressed by the considerably greater excretion of dopamine and, in part, epinephrine, in children 12 to 15 years of age residing in zones of high density of radiation contamination, even in cases of relatively low levels (0.43±0.05 µCi) of radiocesium accretion.

It was also found that greater accretion of radionuclides in children of the first and second groups causes increased excretion in urine of the main metabolite of serotonin, 5-hydroxyindoleacetic acid (from 3.37±0.37 and 3.96±0.13 to 5.09±0.44 and 5.17±0.36 µg/ml, respectively, p<0.05), which is apparently indicative of impaired metabolism of this biogenic amine in tissues also.

The findings indicate that the combination of two factors, high density of contamination of an area and accretion of radionuclides in children, elicits appreciable changes in metabolism of catecholamines and serotonin, and increased excretion in urine of their main metabolic products. Internal accretion of radionuclides is instrumental, to a greater extent, in increased excretion of catecholamine and serotonin metabolites.

The demonstrated increase in excretion of VMA in urine of children with high level of radiocesium accretion is indicative of persistent activation of the adrenosympathetic system and intensification of release in tissues of catecholamines with antioxidant activity, which may be viewed as the body's compensatory metabolic reaction.

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UDC 612.014.482:612.017.1]-053.2(476.2)(476.4)

Evaluation of Immune Status of Children in Zone of High Radiation*907C0862G Minsk ZDRAVOOKHRANENIYE
BELORUSSII in Russian No 6, Jun 90 (manuscript
received 14 Feb 90) pp 33-35*

[Article by N. N. Galitskaya, L. A. Khmelevskaya, G. M. Zhuk, and T. V. Vorontsova, Belorussian Scientific Research Institute of Radiation Medicine]

[Text] The adverse radiation situation that developed after the Chernobyl accident sets medical workers the task of comprehensive investigation of physical condition, including status of the immune system of individuals residing in contaminated areas and, first of all, children living in strictly monitored zones. For this reason, we carried out studies to evaluate the immune status of children in the second monitoring category from Gomel and Mogilev oblasts.

Material and Methods

Immunological status was evaluated on the basis of several tests characterizing the condition of the T- and B-immunity systems, as well as nonspecific constitutional resistance [1, 2, 3]. Assays were made of relative and absolute T- and B-lymphocyte count, levels of T-lymphocyte subpopulation, levels of immunoglobulins in blood serum, circulating complex content. The tested parameters of nonspecific resistance were levels of serum lysozyme and concentration of interferon.

Mathematical analysis of the obtained parameters was carried out by the method of variation statistics with calculation of arithmetic mean, standard deviation (S_x) and representativity error (m_x).

Results and Discussion

The children submitted to immunological testing were first examined by pediatricians and other specialists. Grade I thyroid hyperplasia, without functional impairment was noted in 45 percent. No pathology was demonstrated in the rest of the children. The table lists data on examination in 1987-1988 of children as related to place of residence and age.

Groups of examined children in monitoring category II

Place of residence	Absolute number	Age	
		3-7 years	7-14 years
Bragin urban settlement	70	6	64
Druzhnyy urban settlement	48	11	37
Gomel Oblast (other rayons)	54	12	42
Mogilev Oblast	67	16	51
Children from clean area (control group)	22	7	15
Totals	261	52	209

In assessing the immunological status, attention was given primarily to the T-cell element of immunity, and it was established that absolute and relative T-lymphocyte content did not differ appreciably in children exposed to radiation from the values found in the same groups of children residing in areas without a radiation problem. Relative T-lymphocyte values were within the range of 49.86 ± 1.52 - 53.36 ± 2.58 percent, while the absolute ones constituted 1356 ± 50 - 1460 ± 135 cells/ μ l. In essentially healthy children of the control group (in the city of Minsk) these parameters constituted 53.0 ± 1.89 percent and 1362 ± 97 percent.

No differences were noted in these parameters, as compared to the normal values for the different age groups (3-7 and 7-14 years), as well as tested children from different rayons.

Analogous findings were obtained from an assay of different subpopulations of T-lymphocytes. A comparison of percentage of T-suppressors failed to demonstrate reliable differences between children exposed to radiation and those in the control group. The same applied to the subpopulation of T-active lymphocytes, which did not differ from normal values in all of the tested groups. It should be noted that the white cell count in tested children exposed to radiation was within the same range as in the control group of children. At the same time, some changes were found in different tested groups with reference to complement-dependent B-lymphocytes. Such changes, in particular an increase in B-lymphocytes, were noted in children from the Druzhnyy and Bragin urban settlements. In these groups, B-lymphocyte levels constituted 22.66 ± 2.8 percent and 20.94 ± 0.79 percent, respectively, versus 16.8 ± 0.95 percent in the control. The differences between the above-mentioned groups, as compared to the control, are statistically reliable ($p < 0.05$). In-depth examination of relative B-lymphocyte content revealed that the increase in B-cells in children from Druzhnyy and Bragin were observed primarily in the 3-7 year age groups. In older children, B-lymphocyte content was within the normal range for their age.

There was also some tendency toward increase in serum immunoglobulins G, which was observed primarily in children from Druzhnyy, Bragin and Mogilev Oblast. In children from the two urban settlements, means constituted 13.68 ± 1.22 and 13.23 ± 0.61 , respectively, versus 10.97 ± 2.06 in the control group ($p > 0.05$). The children from Bragin also presented with elevation of circulating immune complex levels (0.087 ± 0.005 , versus 0.06 ± 0.01 in the control). In the rest of the tested children, the levels of circulating immune complexes did not differ from control values. Analogous findings were made for lysozyme (7.44 ± 1.39 for children from Bragin and 9.21 ± 1.88 for those from the city of Minsk). Serum interferon level in the control group of children was 1.6 ± 0.5 U and for children from Bragin it was 10 ± 0.8 U.

It was established that iodine radionuclides made up a significant share of all radionuclides in the first few days after the accident; as we know the former have a selective affinity for thyroid tissues. For this reason, it is desirable to compare immunological indicators separately for the group of children with enlargement of the thyroid, as compared to the control.

Analysis of the findings concerning lymphocyte content, with consideration of existing changes (hyperplasia) in the thyroid, indicates that the parameters did not change appreciably in the presence or absence of such pathology in the older age group (7-14 years) and younger group (3-7 years) of children from Druzhnyy and Bragin urban settlements, as well as in Mogilev and Gomel oblasts. No reliable differences were demonstrated, with consideration of changes in the thyroid and B-lymphocyte content in the older group (7-14 years). At the same time, reliable increase in B-lymphocyte content, which was also unrelated to condition of the thyroid, was found in 3-7-year children from Druzhnyy urban settlement (relocated from Prip'yat urban settlement) and Bragin urban settlement. In the older children from the above-mentioned places, a change was found in serum IgG, in particular, an elevation in children without thyroid hyperplasia (0 stage). In children from Prip'yat these changes were found in girls (19.16 ± 2.2 , versus 11.57 ± 0.69), whereas in Bragin they were demonstrated in boys of the same age group (16.59 ± 0.9 , versus 9.3 ± 0.7). Such changes were not found in children from Mogilev Oblast. At the same time, data were obtained for children from Bragin and Druzhnyy indicative of some correlation between severity of thyroid hyperplasia and serum interferon level.

Thus, our findings on long-term (1.5-2 years after the accident) monitoring of the immune system are indicative of certain changes in some elements of immunity, this applies in particular to the B system of immunity, its activation. It is not deemed possible to determine the cause of these phenomena, let alone offer a concrete interpretation for them at the present time. A more reliable interpretation of the findings can be offered by analysis of the data obtained from dynamic monitoring. At the same time, we know from the literature that expressly the B-cell immunity system reacts sooner to radiation than the T-cell system [4].

At the same time, the findings of long-term monitoring of the immune system of children in monitoring category II show that there are no data indicative of diminished immunity. In addition, the demonstrated activation of some elements of the B-cell immunity system can, with some degree of probability, be a reflection of adaptation processes in the immune system, on the one hand, and indicative of stressed immunity, on the other hand. It is known that the immune system has a powerful potential for adaptation, but it is not unlimited, and for this reason it is necessary to bear in mind that the radiation dose load on the body may increase as time passes, and consequently there may also be a decline in immunity

activity in some cases. Therefore, even now, it is necessary to carry out comprehensive preventive measures to strengthen the immune system.

Conclusions

1. Some dynamics have been found in immunological parameters, indicative of activation of the B-element of the immunity system 1.5-2 years after the accident, in children exposed to radiation.
2. No deviations were demonstrated in parameters characterizing the T-element of immunity.

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UDC 539.16:616-001.28/.29:612.014.482

Cytogenetic Effects of Additional Exposure to Low Doses of Ionizing Radiation

907C0862H Minsk ZDRAVOOKHRANENIYE
BEORUSSII in Russian No 6, Jun 90 (manuscript
received 12 Dec 89) pp 38-41

[Article by G. I. Lazyuk, K. A. Bedelbayeva, and Zh. N. Fomina, Belorussian Scientific Research Institute of Hereditary and Congenital diseases]

[Text] The cytogenetic effects on man of low doses of ionizing radiation have not been sufficiently investigated, whereas no studies at all were carried out about such effects as a result of combined exposure to products of environmental contamination present in the discharge from the Chernobyl AES. The main information on this score was obtained from works based on investigation of chromosome aberrations in peripheral blood lymphocytes of individuals who survived the atomic bombing of Hiroshima and Nagasaki, as well as those exposed to occupational radiation and patients submitted to radiation and x-ray therapy.

Studies of individuals who survived the bombing revealed that the incidence of aberrant cells in peripheral

blood lymphocytes is proportionate to radiation dosage, and that chromosome aberrations persist for at least 3 decades after exposure. Most such aberrant cells had symmetrical exchanges (reciprocal translocations and inversions), whereas the incidence of aberrations (dicentric and rings) was lower by a factor of 10 [6]. The same function of dosage was demonstrated by Sofuni et al. [8] in a later study of individuals who survived atomic bombing and were submitted to total body radiation of 1 to 8.5 Gy from gamma-radiation and neutrons.

The investigations of A. K. Ryabukha et al. [4] make it possible to judge the level and postradiation dynamics of disturbances in the chromosome system of peripheral blood lymphocytes in individuals exposed to radiation. After completion of a course of radiation therapy (70-90 Gy cumulative dose to the target), the number of damaged cells increased from the baseline level of 1.51 to 19.46 percent, the number of aberrations per 100 cells increasing to 29.7. The cited authors note that, for the first 3-5 years, the number of aberrant cells diminishes to almost one-half, with no appreciable decline of these parameters thereafter (up to 9 years). There was 5-6-fold increase in chromosome disturbances and cells with aberrations, as compared to the control, and even when tested after 7-9 years unstable aberrations—dicentric, paired fragments and rings—were observed.

Damage to human chromosomes from low doses of ionizing radiation has been observed by many researchers in individuals who worked for long periods of time with sources of ionizing radiation. Thus, I. A. Zykova et al. [3] examined 47 men who worked under identical conditions of fluctuating microclimate, and were exposed to 1.82 ± 0.14 rem gamma-radiation annually for the last 3 years. Overall incidence of aberrations was 2.64 ± 0.41 percent in the older individuals, 1.09 ± 0.30 percent in younger workers, versus 1.00 ± 0.18 and 1.03 ± 0.32 percent, respectively, in the control. Evans et al. [7] demonstrated a about 1 dicentric chromosome per 700 cells in peripheral blood lymphocytes in deckyard workers exposed to mixed radiation from neutrons and gamma-rays (fueling nuclear reactors of submarines) in a dosage of less than 0.01 Sv [Sievert]/year, and about 4 times more such chromosomes after cumulative doses of 0.2-0.3 Sv. Sensitivity of chromosomes in human peripheral blood lymphocytes was used as a possible biological dosimeter of acute exposure, and it was recommended by WHO as a test system for evaluation of the effect of environmental mutagenic factors on human heredity.

Material and Methods

Lymphocytes from peripheral blood of individuals living in Gomel Oblast (Khoynikskiy, Braginskiy and Narovlyanskiy rayons) and Mogilev Oblast (Slavgorodskiy, Krasnopol'skiy, Cherkovskiy, Kostyukovichskiy, Klimovichskiy rayons) served as the material for this cytogenetic study. All subjects were divided into several groups. The first group consisted of 51 parturients from Narovlyanskiy and Khoynikskiy rayons of Gomel Oblast who were evacuated to Novopolotsk. The second group

consisted of 34 neonates delivered by the first group of parturients. Both groups were examined to assess the cytogenetic effects of acute exposure to ionizing radiation, the doses of which were received primarily from radioactive iodine. To study the dynamics of levels of chromosome aberrations in the above groups, we succeeded in re-examining 5 parturients and 5 neonates [3d and 4th groups]. The other groups consisted of individuals submitted to chronic exposure to low doses of radiation. Thus, the fifth group was represented by 25 pregnant women living in Vetka urban settlement in Gomel Oblast, who had been in the contaminated zone for about 10 months prior to the chromosome study. The sixth group consist of 15 parturients from the most contaminated rayons of Mogilev Oblast, and blood samples were taken 8 months after the accident. The seventh group consisted of neonates delivered by the sixth group of parturients. Additional examination of 8 parturients (8th group) and 16 neonates (9th group) from different rayons of Mogilev Oblast was performed 2 years after the Chernobyl accident. As a control we took 18 women from Novopolotsk and 21 neonates from the city of Grodno.

Venous and umbilical blood lymphocytes were cultured by conventional methods. Cultivation lasted 48 h. The preparations were stained with azure-eosin for 5 min. A total of 300 metaphases were analyzed from each individual. Metaphase plates were collected in accordance with the criteria proposed by N. P. Bochkov [1]. Chromosome aberrations were recorded using conventional techniques [1, 2, 5].

Results and Discussion

One must know the quantitative patterns of appearance of radiation-induced chromosome aberrations for proper prediction of the effect of radiation on human heredity. The most convenient way of expressing the mutation effect is to compare the incidence of induced mutations to that of spontaneous mutations.

Observation of cytogenetic effects in parturients of Gomel Oblast tested in 1986 and 1988 revealed reliable increase in total number of aberrations (1.45 ± 0.10 percent and 2.27 ± 0.38 percent, respectively), and this increase pertained primarily to chromatid aberrations. Mean incidence of aberrations in the control group of women from Novopolotsk constituted 1.34 ± 0.16 percent (0.81 ± 0.12 percent chromatid type, 0.53 ± 0.10 percent chromosome type). An increase in chromosome mutation was observed in cultures of lymphocytes from parturients of both groups (1.00 ± 0.09 percent and 1.20 ± 0.28 percent), as compared to the control group (0.53 ± 0.10 percent). The total number of aberrations was reliably higher, constituting 3.15 ± 0.20 percent ($P_1=0.99$), for both chromatid and chromosome types of aberrations (1.49 ± 0.14 percent and 1.66 ± 0.15 percent), in the group of pregnant women tested in 1987. Comparative analysis of the incidence of chromatid and chromosome aberrations in neonates, who were also tested repeatedly, revealed that the total incidence of

aberrations at the second examination in 1988 (1.90+/-0.35 percent) was reliably higher than in 1986 (1.13+/-0.12 percent); the increase was referable primarily to aberrations of the chromatid type.

Cytogenetic studies of parturients and neonates in Mogilev Oblast were conducted in 1986 and 1988. In parturients tested in 1986, total incidence of chromosome aberrations (1.57+/-0.19 percent) of both the chromatid (0.88+/-0.15 percent) and chromosome (0.69+/-0.13 percent) types was lower ($P_1=0.99$) than in the group of women retested 2 years later (2.51+/-0.18 percent; 1.39+/-0.13 percent; 1.12+/-0.12 percent). A study of incidence of chromosome aberrations in neonates revealed that

more aberrations were noted in the group of infants tested in 1988 (2.57+/-0.21 percent) than in 1986 (1.51+/-0.16 percent). It should be noted that the increase in total number of aberrations occurred primarily due to chromatid aberrations (the ratio of chromatid to chromosome type was 2.2:1.0).

The total number of aberrant cells, number of all aberrations, presence of dicentric and ring chromosomes are among the most objective indicators in biological dosimetry [5]. A comparison of these indicators in different groups of tested individuals was made for quantitative and qualitative evaluation of changes in them. Summary data are listed in Tables 1 and 2.

Table 1. Incidence (percent) of main indicators of chromosome aberrations in blood lymphocyte culture, in parturients, neonates and pregnant women in Gomel Oblast

Group	Metaphases tested	Aberrant cells	Paired fragments	Dicentrics+rings
Parturients				
—1986	13135	0.69+/-0.07	0.66+/-0.07	0.18+/-0.04
—1986	1510	0.86+/-0.23	0.72+/-0.22	0.40+/-0.16
—1988	1500	0.66+/-0.20	0.46+/-0.17	0.40+/-0.16
Pregnant women (1987)	7500	1/54+/-0.14	1.50+/-0.14	0.14+/-0.04
Neonates				
—1986	7866	0.72+/-0.10	0.52+/-0.08	0.22+/-0.05
—1986	1301	0.38+/-0.17	0.07+/-0.07	0.38+/-0.17
—1988	1480	0.34+/-0.15	0.20+/-0.12	0.14+/-0.10
Control (Novopolotsk parturients)	5310	0.51+/-0.09	0.47+/-0.09	0.04+/-0.03
Control (Grodno neonates, 1987)	6300	0.68+/-0.10	0.58+/-0.09	0.15+/-0.05
Control (Moscow, A. V. Sevankayev, 1987)	30000	—	0.38+/-0.04	0.02+/-0.008

Table 2. Incidence (percent) of main indicators of chromosome aberrations in blood lymphocyte culture, in parturients and neonates in Mogilev Oblast

Group	Metaphases tested	Aberrant cells	Paired fragments	Dicentrics+rings
Parturients				
—1986	4079	0.63+/-0.12	0.59+/-0.12	0.10+/-0.05
—1988	7715	1.10+/-0.12	0.93+/-0.11	0.19+/-0.05
—1986-1988	11794	0.92+/-0.09	0.81+/-0.08	0.16+/-0.04
Neonates				
—1986	5961	0.65+/-0.10	0.59+/-0.10	0.13+/-0.05
—1988	5640	0.26+/-0.07	0.11+/-0.04	0.21+/-0.06
—1986-1988	11601	0.46+/-0.06	0.35+/-0.05	0.17+/-0.04
Control (Novopolotsk parturients)	5310	0.51+/-0.09	0.47+/-0.09	0.04+/-0.03
Control (Grodno neonates, 1987)	6300	0.68+/-0.10	0.58+/-0.09	0.15+/-0.05
Control (Moscow, A. V. Sevankayev, 1987)	30000	—	0.38+/-0.04	0.02+/-0.008

Comparative analysis of the incidence of the main indicators of chromosome aberrations in cultures of

blood lymphocytes from the two groups of parturients and neonates in Gomel Oblast tested in 1986 and 1988

(Table 1) failed to demonstrate reliable differences, either in aberrant cells (0.86 ± 0.23 percent, 0.66 ± 0.20 percent and 0.38 ± 0.17 , 0.34 ± 0.15 percent, respectively) or in indicators of dicentric and ring chromosomes (0.40 ± 0.16 percent, 0.40 ± 0.16 percent, and 0.38 ± 0.17 percent, 0.14 ± 0.10 percent, respectively). We were impressed by the high incidence (1.54 ± 0.14 percent) of aberrant cells in pregnant women tested in 1987. As can be seen from the data listed in Table 1, all of the tested individuals in Gomel Oblast, as well as neonates taken as a control from the city of Grodno, presented with a high incidence of dicentric and ring chromosomes, as compared to the control group of women from Novopolotsk (0.04 ± 0.03 percent). The rise in incidence of dicentric and ring chromosomes in neonates from Grodno is apparently related to the adverse ecological conditions.

Table 2 lists data from cytogenetic analysis of the main parameters considered in biological dosimetry for women and infants in Mogilev Oblast. A comparison of the two groups of parturients tested in 1986 and 1988 revealed reliable ($P_1=0.95$) increase in incidence of all types of chromosome aberrations in the group of women who had remained in the contaminated area for a longer time. Neonates (1986-1988) showed reliable ($P_1=0.95$) decline of aberrant cells and paired fragments (Table 2). Overall data (1986-1988) for dicentrics and rings were reliably higher in both parturients (0.16 ± 0.04 percent) and neonates (0.17 ± 0.04 percent) than in the control group of women from Novopolotsk (0.04 ± 0.03 percent).

Conclusion

Thus, the studies revealed that both the pregnant women evacuated from Bragin and Khoynikov urban settlements and pregnant women at least 150 km away from the Chernobyl AES were exposed to biologically effective doses of radiation, as manifested by increase in total number of aberrant blood cells, as well as increased percentage of dicentrics and rings. However, the cumulative mutagenic effect was less marked in the evacuated women than in those living in the contaminated zone more than 150 km away from Chernobyl.

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UDC 612.014.482:611-018.54]-053.5(476.2)(476.4)

Status of Interferon System of Schoolchildren Living in Braginskiy and Cherikovskiy Rayons of Belorussia

907C0862I Minsk ZDRAVOOKHRANENIYE
BELORUSSII in Russian No 6, Jun 90 (manuscript
received 14 Feb 90) p 48

[Article by I. V. Korobko and L. P. Titov, Minsk]

[Text] Extensive information has been accumulated to date concerning the interferon system and its role in homeostasis. Numerous studies have demonstrated that interferon can stimulate or suppress specific immunity and factors pertaining to nonspecific protection [2, 3].

By altering plasma membranes, interferon causes intensification of cell immunity, as manifested by stimulation of phagocytosis, increase in cytotoxicity of naturally occurring killer cells, increased expression of surface antigens, etc. At the same time, the effect of high concentrations of interferon on B- and T-lymphocytes usually leads to immunosuppression [4].

The most accessible overall indicators of interferon in the body is quantitative assay of this protein, which circulates in blood, or assay of so-called serum interferon.

Our objective here was to determine the status of the interferon system of school-age children living in areas of high radioactivity (Braginskiy and Cherikovskiy rayons).

Blood serum from 366 essentially healthy children (160 from Braginskiy and 206 from Cherikovskiy rayons) served as our material.

In order to determine the activity of serum interferon, we used the method of suppression of cytopathic activity of a test virus (vesicular stomatitis virus, Indiana strain) in a culture of diploid cells from a human embryo. The reciprocal of the dilution of interferon providing 50-percent protection of monolayer cells against the cytopathic effect of the test virus served as the unit of interferon activity.

The assay of titers of circulating (serum) interferon revealed that no interferon was demonstrable in the serum of 18.7 percent of the tested children from Braginskiy Rayon. In 55 (34.4 percent) of the subjects, interferon titers constituted 4-8 IU. Interferon titers were 16-32 IU in 69 (43.2 percent) and exceeded 32 IU in 6 (3.7 percent) children.

Assays of circulating interferon titers in children living in Cherikovskiy Rayon revealed that 60 (29.1 percent) of the subjects showed no serum interferon. In 40.2 percent (83 subjects) of the children, interferon titers constituted 4-8 IU. They equaled 16-32 IU in 54 (26.2 percent) children and exceeded 32 IU in 9 (4.6 percent).

At the same time, according to our own findings and data in the literature [1], testing of circulating interferon in blood serum of healthy donors revealed that none was demonstrable in 75 percent. Interferon titers constituted 4-8 IU in 13 percent of the donors, i.e., they corresponded to the baseline levels. In 12 percent, circulating interferon titers reached 16-32 IU, i.e., they exceeded insignificantly the normal baseline level.

Thus, in 75 percent of the cases no interferon was demonstrable in circulating blood of healthy subjects, whereas in the tested children it was found in only 18.7 and 29.1 percent of the cases, respectively. Serum interferon level was at the baseline level in 13 percent of the healthy subjects, but constituted 34.4 and 40.2 percent of the children tested from the rayons with high radiation background. Interferon levels insignificantly above the normal baseline were observed in 12 percent of the healthy subjects, in 43.2 and 26.2 percent of tested subjects from the two rayons.

It is a known fact that the action of interferon in the overall system of homeostasis is aimed at protecting the body against penetration of foreign genetic information, as well as protection of its own genetic material against the destructive effect of radiation; since interferon is the only naturally occurring radioprotective agent that is synthesized right in the body, an increase in its level in the blood of the tested group could serve as the body's response to radiation.

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UDC 6127.1:612.11(476.2)"1983-1988"

Dynamics of Peripheral Blood Morphology in Residents of Gomel Oblast in 1983-1988

907C0862J Minsk ZDRAVOOKHRANENIYE
BELORUSSII in Russian No 6, Jun 90 (manuscript
received 14 Feb 90) pp 49-50

[Article by V. A. Syatkovskiy, Ye. R. Linkevich, L. A. Azarova, I. V. Korobko, L. A. Krylova, A. I. Nemets, and L. F. Smorshchok, Minsk]

[Text] The ecological and social condition under which man lives is undergoing the most marked deformations in the 20th century. Among such factor radiological background is presently becoming increasingly active.

The normal functional parameters of human organs and systems are undergoing some changes under the influence of the complicated set of factors.

The hemopoietic system is among the most radiosensitive systems. This investigation deals with dynamics of morphological composition of peripheral blood in essentially healthy residents (ranging in age from 18 to 50 years) of Gomel Oblast in 1983-1988. The choice of this period was made for the following reasons. In the first place, more than 10 years have passed since the last publication concerning normal peripheral blood composition in the population of Belorussia; in the second place, the dramatic change in radiation conditions in Gomel Oblast in 1986 made it possible to carry out a comparative study of hemopoiesis before and after the accident at the Chernobyl AES [nuclear power plant].

We analyzed data on peripheral blood morphology in a total of 13,297 essentially healthy male and female residents of Gomel Oblast in 1983-1988 (716 in 1983, 1550 in 1984, 2210 in 1985, 2002 in 1986, 2783 in 1987, 4036 in 1988). Analysis was made of data for each month. The size of the monthly samplings ranged from 41 to 433 people.

We studied the following parameters: red blood cell count, hemoglobin content, color index, white cell and thrombocyte count, differential count and erythrocyte sedimentation rate [ESR].

We assayed peripheral blood parameters of 8597 essentially healthy individuals residing in the city of Minsk as a control group. Mean values of the main peripheral blood parameters of the tested groups are listed for each year in Tables 1 and 2.

Table 1. Indicators of peripheral blood morphology in residents of Gomel Oblast

Year	Values						
	hemoglobin	erythrocytes	leukocytes	stab	ESR	reticulocytes	thrombocytes
1983	145.54	4.58	6.50	0.95	5.4	1.52	200.5
1984	148.00	4.66	6.34	1.04	5.6	3.16	191.8
1985	150.56	4.54	6.47	1.65	5.3	2.99	205.8
1986	152.40	4.60	6.03	2.10	4.6	2.44	219.7
1987	152.89	4.58	6.10	1.75	4.8	2.27	217.5
1988	154.29	4.54	6.16	1.76	3.9	2.89	201.7

Table 2. Indicators of peripheral blood morphology in residents of Minsk

Year	Values				
	hemo- globin	leuko- cytes	stab	mono- cytes	ESR
1984	141.65	5.78	1.15	2.50	5.45
1985	139.25	5.82	0.73	0.18	4.81
1986	137.15	5.46	0.51	1.81	4.36
1987	137.79	5.55	0.75	1.57	4.50
1988	138.67	5.57	0.75	0.60	4.70

Analysis of the obtained data revealed that no pathological changes were observed in peripheral blood of the population of Gomel Oblast in 1983-1988. We also failed to demonstrate appreciable changes in parameters of peripheral blood or development of overt tendencies over the survey period. Rise in hemoglobin level in 1983-1988 and decline of ESR, low white and lymphocyte counts in peripheral blood can be mentioned among the trends. It is necessary to note that the monthly fluctuations of different parameters of peripheral blood over the observation period were also insignificant. As we know, lymphocytes are the most radiosensitive peripheral blood cells. There was monthly fluctuation of peripheral blood lymphocytes. We also failed to demonstrate any appreciable changes in thrombocyte count. As can be seen from the tables, there are also no appreciable differences in peripheral blood values between residents of Gomel Oblast and Minsk.

At the same time, preliminary analysis of seasonal changes in peripheral blood parameters enabled us to detect a high hemoglobin level and thrombocyte count in the third quarter of the year. Leukocyte count was somewhat higher in the fall and winter period than in the spring and summer. It was somewhat higher in the summer than in the fall.

Thus, analysis of peripheral blood morphology in residents of Gomel in 1983-1989 and residents of Minsk revealed that the parameters studied did not undergo any appreciable changes over the indicated period. It was noted that some parameters (hemoglobin, thrombocytes, leukocytes) were a function of time of year.

At the same time, the results of these population studies do not mean that it would be expedient to carry out

in-depth studies in this direction. In particular, the turn from morphological parameters of peripheral blood, which could be viewed as being relatively stable, to more sensitive functional tests characterizing the status of hemopoiesis could yield important information about development of prepathological states, i.e., preclinical forms of functional change in the hemopoietic system.

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UDC 577.391:612.6:613.648-07(476)

Incidence of Developmental Defects in Human Embryos in Different Regions of Belorussia

907C0862K Minsk ZDRAVOOKHRANENIYE
BELORUSSII in Russian No 6, Jun 90 (manuscript
received 12 Dec 89) pp 53-55

[Article by I. A. Kirillova, I. V. Novikova, N. N. Arydov, and B. V. Nalibotskiy, Belorussian Scientific Research Institute of Hereditary and Congenital Diseases]

[Text] It is known that human embryos and fetuses are more sensitive to deleterious environmental factors than neonates or adults. A study of children exposed prenatally to radiation in Nagasaki and Hiroshima, as well as outcome of pregnancies in women after receiving radiation therapy, indicates that fetal radiosensitivity is inversely proportionate to age [5]. A screening of 50,000 neonates, whose parents were exposed to the nuclear explosion, revealed developmental defects in 1.4 percent, whereas the figure was 1.18 percent in the control (those not exposed to radiation); microcephaly, hydrocephalus and heart defects were the most frequent findings [9]. Analysis was made of the sequelae of radiation therapy of the pelvic region of 200 pregnant women in the 4th-25th weeks of gestation; the most frequent developmental disturbances in the infants they delivered were microcephaly accompanied by mental retardation, microphthalmos, degeneration of retinal pigment layer, skeletal and reproductive system defects [8]. It was shown that the fetal brain is particularly sensitive to radiation when exposed between the 8th and 15th gestation weeks [3]. Lower birth weight and length was demonstrated after single exposure to diagnostic x-rays of 152 women in the second week of gestation [10]. There are contradictory data concerning the link between exposure to radiation and chromosome pathology [2]. In some investigations, it is concluded that irradiated parents have a greater chance of giving birth to infants with Down's syndrome [3]. However, analysis of chromosome aberrations in infants whose parents survived atomic bombing failed to demonstrate reliable differences from a control group of patients, although data pertaining to 7540 infants were analyzed [6]. Nor were any radiation effects found in offspring of radiologists [7]. N. P. Bochkov [1] believes that such contradictions are related to the fact that it is difficult to gather data on radiation effects in a single laboratory, since a large sample is needed. It was concluded by the Scientific Committee on the Effects of Atomic Radiation (NCEAR) that, thus far, there are no reliable quantitative estimates of the risk of human embryo exposure in the case of low dose levels [2].

There is a well-known triad of effects in experimental technology, which are observed with exposure of the fetus to ionizing radiation: developmental defects, growth retardation and early embryo death [4]. Such effects have been less studied in clinical teratology, whereas the effects of low doses, and those received as a result of combined radiation exposure have not been investigated alone, so that it is impossible to predict the sequelae of additional exposure of large groups of people or to plan specialized medical genetic care, and makes it difficult to offer medicogenetic counseling for individuals exposed to different doses of ionizing radiation.

With this in mind, our objective here was to demonstrate the teratogenic and combined (teratogenic and mutagenic) effects of combined exposure to ionizing radiation on man by the method of recording developmental

defects in embryos aborted from residents of southern regions of Belorussia as a result of the Chernobyl accident.

Material and Methods

The material for our study consisted of human 4-12-week embryos aborted in the second half of 1986, in 1987 and in the first half of 1988 in the cities of Minsk and Gomel, as well as southern rayons of Gomel and Mogilev oblasts: Khoynikskiy, Braginskiy, Narovlyanskiy, Krasnopol'skiy, Klimovichskiy, Kostyukovichskiy, Slavgorodskiy and Cherkovskiy. Table 1 lists the quantitative data. As a control, we used 10,168 human embryos at the same stage of prenatal development, which were taken at random following medical abortions in the city of Minsk during the period from 1980 to 1985.

Material was collected in sterile vials with Hanks' solution. Diagnosis of developmental defects in embryos was made by microdissection under an SM-XX stereomicroscope in Petri dishes with sterile Hanks' solution. A technique developed in our laboratory was used, which included a specific sequence of operations. The age of the embryos was determined with consideration of the Carnegie stage. Abnormally formed organs were photographed, preparations made, measured and, in a number of instances, the diagnosis was verified by means of examining serial histological sections after passage through a series of alcohols, embedding in paraffin and hematoxylin-eosin staining. Appropriate growth curves with plotted confidence intervals were used to diagnose hypoplasia of different organs.

Information about the incidence of defects was submitted to statistical processing, using the SM 1403 computer, in the Laboratory of Morphological Examination Methods (chief: A. Ya. Rubenchik) at the Minsk Medical Institute. The staff of this laboratory developed a method for eliminating the effect of the age factor on incidence of defects.

Results and Discussion

Table 1 lists information about the incidence of developmental defects in embryos in different regions of Belorussia. We see that the overall incidence of developmental abnormalities in aborted embryos in the cities of Minsk (5.0 ± 0.5 percent) and Gomel (4.3 ± 0.8 percent) following the Chernobyl accident did not differ from the same indicators in the control sample (5.64 ± 0.30 percent; $p > 0.05$). A comparison of the incidence of defects found in May-June 1986, the teratogenetic termination period of which coincided with the time of maximum radiation exposure, and developmental abnormalities that occurred in Minsk in the subsequent period failed to demonstrate statistically reliable differences ($p > 0.05$).

Table 1. Incidence (percentage) of developmental defects in aborted fetuses in some regions of Belorussia

Parameters	City of Minsk		City of Gomel	Southern rayons of Mogilev Oblast	Southern rayons of Gomel Oblast	Southern rayons of both Gomel and Mogilev oblasts
Date of sampling	1980-1985	2d semester, 1986-1987	2d semester 1986-1987	2d semester 1986-1st semester 1988	2d semester 1986-1st semester 1987	2d semester 1986-1st semester 1988
Total cases	10168	2861	1595	482	91	573
—including informative ones	5732	1920	674	158	38	196
Number of aborted fetuses with developmental defects	321	96	29	13	5	18
Incidence of developmental defects, percent	5.6+/-0.3	5.0+/-0.5	4.3+/-0.8	8.2+/-2.2	13.2+/-5.5	9.2+/-2.1
Reliability of differences from the city of Minsk, 1980-1985:						
—t		1.00	1.40	1.40	2.00	2.13
—p		>0.05	>0.05	>0.05	<0.05	<0.05

In the time that has elapsed since the accident there has been no noticeable change in spectrum of developmental defects. Nor was there any rise in incidence of nosological forms inherent in radiation exposure.

A comparison to the control of incidence of developmental defects in embryos in southern rayons of Mogilev Oblast revealed that, although the mean values were above the control, the differences were unreliable ($p > 0.05$). The increase in developmental defects in southern rayons of Gomel Oblast was found to be statistically significant ($p < 0.05$). Overall incidence in defects in southern parts of Gomel and Mogilev oblasts was also reliably higher than in the control ($p < 0.05$). However, we failed to demonstrate developmental disturbances relatively typical of radiation exposure in the spectrum of the developmental defects recorded in these rayons.

Since it is known that the incidence of developmental defects in human embryos declines with age, by virtue of spontaneous elimination of abnormal embryos, we used the method of elimination of effect of the age factor on incidence of defects in different samples. The standardized incidence of developmental abnormalities in southern rayons of Gomel and Mogilev oblasts (9.88 ± 2.57 percent) is reliably ($p < 0.05$) higher than in the control (3.62 ± 0.31 percent). Consequently, the recorded rise in incidence of developmental defects in embryos in the zone of radiation contamination is not related to the age composition of the tested sample. After the accident, the normalized incidence of defects in the city of Minsk constituted 4.17 ± 0.48 percent ($p > 0.05$).

Investigation of the spectrum of defects in the radiation contaminated zone enables us to voice some suggestions

concerning mechanisms of radiation teratogenesis after exposure to low doses of ionizing radiation. As we know, one of the typical radiobiological embryonic reactions is destruction of some number of cells of organ primordia [4], which should have led to an increase in defects of the hypoplastic type. The absence of increase in such abnormalities according to our findings does not allow us to confirm the possibility of this route of onset of defects with the doses of ionizing radiation present in our case.

The increased incidence of developmental defects in our material occurred due to a group of multifactorial defects, the onset of which is described by polygenic models with a threshold effect. One could think that ionizing radiation, being an environmental component in the complex etiology of such defects, lowers the threshold with subsequent impairment of shape-forming processes. Further studies are needed to define the role of other factors, in particular demographic and ecological ones, which affect the incidence of developmental defects.

Conclusions

1. Overall incidence of developmental defects in medically aborted embryos in the cities of Minsk and Gomel following the accident at the Chernobyl AES does not differ reliably from the indicator for a control sample.
2. A reliable rise in incidence of defects was recorded in human embryos in southern rayons of Gomel Oblast, and in overall incidence of defects in southern rayons of Gomel and Mogilev oblasts.
3. The incidence of developmental defects, normalized for embryo age, in southern rayons of Gomel and Mogilev oblasts is reliably higher than control values; consequently, the recorded tendency toward rise in incidence of defects is unrelated to the age structure of the sample studied.

4. No increase was demonstrated in defects relatively inherent in radiation exposure.

5. The record of developmental defects in human embryos can be used by health care agencies as a high-speed method of evaluating the effects on man of various teratogenic and mutagenic factors.

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UDC 616-053.31-007.053.1(476.2)(476.4)

Monitoring Congenital Developmental Defects in Neonates of Southern Rayons of Gomel and Mogilev Oblasts

907C0862L Minsk ZDRAVOOKHRANENIYE
BELORUSSII in Russian No 6, Jun 90 (manuscript
received 12 Dec 89) pp 55-57

[Article by G. I. Lazyuk, D. L. Nikolayev, and Ye. G. Ilyina, Belorussian Scientific Research Institute of Hereditary and Congenital Diseases]

[Text] It is well-known from experimental teratology that additional exposure to ionizing radiation at specific stages of the gestation period and in specific doses induces congenital developmental defects [1, 4]. Congenital defects resulting from exposure to radiation may be a manifestation of teratogenic, mutagenic or combined effects. There are few reliable data on the teratogenic effect (formation of congenital defects as a result of exposure to a deleterious factor during pregnancy) on man of ionizing radiation. Most often, such data are either without sufficient validation or contradictory. At the same time, there are numerous reports of the teratogenic effect of radiation on experimental animals [1, 3]. It is believed that the teratogenic radiation dose for man is in the range of 5-10 rem within the first three months of the gestation period [4].

In contrast to the teratogenic effect, where the deleterious factor has a direct influence on the embryo, in the case of a mutagenic effect congenital developmental defects are formed as a result of a deleterious factor (in this case, radiation) affecting the genetic system, i.e., chromosomes of reproductive cells of future parents. It is believed, but not unquestionably, that any dose of ionizing radiation can induce a mutation, while the number of mutations is a function of cumulative dose, dose rate, type of radiation (genetic effectiveness of fast neutrons is 2-6 times greater than that of x-rays) and exposure time [2]. Thus, with chronic exposure the mutagenic effect is one-half to one-third lower than with acute exposure. It has been shown that with a cumulative ionizing radiation dose of 1 Gy delivered at a low dose rate, one can expect about 240 more neonates in the first generation with disease caused by chromosome pathology, and more than 1500 additional cases of genetic disease per million births [3].

Combined effects consist of radiation mutagenesis and additional factors affecting the embryo. Radionuclides incorporated in the mother, toxic chemicals (pesticides, nitrates), hormonal disorders, unbalanced diet, diminished immunity may be such additional factors. The etiology of a group of multifactorial congenital developmental defects (CDD), which are the most frequent CDD, is related to combined factors. Several estimates were made on the basis of data obtained in animal experiments, mainly on mice; however, in view of the difference between human and animal radiosensitivity it

is by far not always that extrapolation of the results of experimental teratology to medical research is justified. There is more validity to make comparisons to data obtained in Hiroshima and Nagasaki. But again, a number of differences related to the sequelae of the atomic bomb (assortment of radionuclides, dose loads, time and other factors) and radionuclide contamination of the environment as a result of anthropogenic factors limits the possibilities for comparison.

At the same time, in view of the constant increase in environmental pollution by chemicals and radionuclides, systems of monitoring the biological consequences of pollutants have been devised in developed countries. One of these systems is genetic monitoring, which is operational in BSSR at the Belorussian Scientific Research Institute of Hereditary and Congenital Diseases. This monitoring system is used for keeping

regular records of births of infants with certain CDD at all of the maternity institutions of this republic. Records are kept on rather frequent CDD, primarily those of known etiology that are identified unequivocally regardless of hospital facilities and qualification of personnel. They include all multiple CDD, Down's syndrome, anencephaly, polydactyly, cleft lip and palate, reduction CDD of the extremities, esophageal and anal atresia.

In order to determine the possible genetic sequelae of the Chernobyl accident, investigations were deployed of embryos from women in the stricken regions of BSSR, mutations of chromosomes in somatic cells of pregnant women, parturients and neonates from the same regions, in addition to the study of incidence of CDD in neonates using the genetic monitoring system.

The table lists the information obtained with the monitoring system.

Incidence of birth of infants with CDD subject to strict monitoring (per 1000 neonates) in southern rayons of Gomel and Mogilev oblasts in 1984-1988

Rayon	1984-1985		1986 (2d semester)-1988 (1st semester)	
	absolute number	per 1000	absolute number	per 1000
Gomel Oblast				
Braginskiy, Buda-Koshelevskiy, Vetkovskiy, Dobrushskiy, Yelskiy, Lelchitskiy, Kormyanskiy, Loyevskiy, Narovlyanskiy, Khoynikskiy, Checherskiy	56	4.55+/-0.61	93	7.66+/-0.79
Petrikovskiy (control)	7	4.47+/-1.69	10	5.33+/-1.68
Mogilev Oblast				
Bykhovskiy, Klimovichskiy, Kostyukovichskiy, Slavgorodskiy, Krasnopol'skiy, Chervinskoy	22	3.68+/-0.78	41	5.61+/-0.87
Goretskiy (control)	8	4.23+/-1.49	11	4.94+/-1.48
Totals for strictly monitored zones	78	4.27+/-0.48	134	6.89+/-0.59
BSSR (excluding above rayons)	1691	5.04+/-0.12	2274	5.65+/-0.12

As can be seen in the table, the incidence of births with CDD in the 17 rayons of Gomel and Mogilev oblasts with the greatest radionuclide contamination rose from 4.27+/-0.48 in 1984-1985 to 6.89+/-0.59/1000 births in 1986-1988 ($t=1.96$). It is premature to attribute the rise in incidence of CDD in the contaminated rayons to radiation, since rises in incidence of CDD in different rayons of BSSR had also been observed prior to the Chernobyl accident, and they were comparable to the higher indicators in 1986-1988 in the contaminated areas. For example, this indicator constituted 7.11+/-1.89/1000 in the control Goretskiy Rayon, whereas the overall incidence of BSSR in this period was 5.65+/-0.13/1000. A rise in incidence of CDD analogous to the most contaminated rayons of Gomel Oblast was noted in the post-accident period in "clean" rayons of Vitebsk Oblast (Polotskiy and Novopolotskiy).

Moreover, no rise in incidence of central nervous system CDD, which are relatively typical of radiation teratogenesis, was demonstrable in neonates in the strictly monitored rayons. Nor did we observe an increase in cases of CDD caused by new dominant mutations. The increase

in CDD occurred primarily due to multifactorially inherited pathology, to the etiology of which deleterious chemical factors make an important contribution. Conversely the incidence of Down's syndrome (the most frequent syndrome caused by mutations) dropped to 0.51+/-0.16/1000 in 1986-1988, whereas in 1984-1985 it constituted 1.04+/-0.24/1000. This decline is related essentially to demographic changes in strictly monitored regions with respect to the share of parturients over 34 years old for whom the incidence of births with Down's syndrome is substantially higher than in young women.

Thus, our investigations of possible genetic consequences of the accident at the Chernobyl AES in the inhabitants of Belorussia enable us to draw the following conclusions.

1. It was established that there was a rise in 1986-1988 in congenital developmental defects in neonates in strictly monitored zones of Mogilev and Gomel oblasts.
2. The increase in incidence of CDD can be tentatively attributed to the effect of a set of factors (radiation, chemical and others not yet identified), as indirectly

indicated by the increase in chromosome mutations in pregnant women and neonates both in strictly monitored zones and "clean" zones with respect to radiation but with high levels of chemical pollution (Novopolotsk, Grodno), and rise in incidence of such defects in Polotsk and Novopolotsk to the same level as in radiation contaminated rayons.

3. For definitive conclusions, further observation by epidemiologists and geneticists and comprehensive evaluation of their findings are needed.

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UDC 616-006.6+616.155.392]-02:614.73(476)

Prediction of Long-Term Oncological and Hematological Diseases Following the Accident at the Chernobyl Nuclear Power Plant

907C0862M Minsk ZDRAVOOKHRANENIYE
BELORUSSII in Russian No 6, Jun 90 (manuscript
received 13 Mar 90) pp 57-60

[Article by Ye. P. Ivanov, K. I. Gorelchik, V. S. Lazarev, and O. M. Klimovich, Belorussian Scientific Research Institute of Hematology and Blood Transfusion]

[Text] According to the data of the physics department at Bremen University (FRG), the collective dose in different parts of FRG ranged from 9×10^6 to 72×10^6 man-rem. This corresponds to 10,000-500,000 cases of death due to oncological diseases (in the next 50 years); the most probable projection is believed to be 250,000 cases (which, if scaled to BSSR, would correspond to 41.667 cases, i.e., there would be 833 additional deaths per year due to radiation exposure). A rise in mortality would be observed due to intake of ^{137}Cs and ^{90}Sr isotopes with food, since 1 Bq ^{137}Cs per liter of milk increases mortality rate by 60 people per million population per year; 1 Bq ^{90}Sr per liter milk increases the death rate by 400 people per million per year [6].

On the basis of these data and measurement of levels of ^{137}Cs and ^{90}Sr activity in food, over a 50-year period one should expect 100,000-200,000 additional cases of death in FRG due to nononcological diseases, which would correspond to 16,667-33,333 deaths in BSSR, i.e., 300 to 700 deaths per year.

In his article, "Chernobyl and Epidemiology of Cancer," R. R. Jones [8] cites the following projections of number of deaths due to cancer caused by ionizing radiation, according to the old data of the Scientific Committee for Radiation Protection (NKRZ) and new estimates of the International Commission for Radiological Protection (ICRP): 125 deaths due to cancer per 10,000 man-Sv [Sievert] (estimates before 1980), 501 deaths (1980 estimates), 1000 deaths (estimates made after 1980).

The collective radiation exposure doses to the population of FRG reached 360,000 man-Sv. This corresponds to 36,000 deaths.

The collective doses to the thyroid constituted 82,000 man-Sv, which corresponds to 2500 deaths due to thyroid cancer (300 deaths due to thyroid cancer per 10,000 man-Sv).

According to our conversions of the data of R. R. Jones, it is expected that there will be 14,028 deaths due to cancer in BSSR over a 50-year period due to intake of ^{137}Cs (on the basis of 1980 estimates) and 28,000 deaths (i.e., about 560 cases per year) according to data obtained after 1980.

The collective dose for all of the European part of the USSR (75 million inhabitants) was 2.1 million man-Sv. Of this dose, 280,000 man-Sv was referable to BSSR.

While the number of deaths in BSSR due to oncological diseases would be, according to these data, 28,000 over a 50-year period, it is expected that there will be an additional 4000 deaths due to oncological diseases (conversion of data in [3]) as a result of external irradiation (collective dose 40,000 man-Sv). Thus, the overall number of deaths would be 32,000.

The death rate we predict due to oncological and nononcological diseases, calculated on the basis of the data for FRG cited by J. Scheer [6], should be increased by 2-4 times for Belorussia (due to its closeness to the accident site), and will constitute 83,334-166,668 cases (oncological) and 33,334-133,332 (nononcological), respectively.

The above projections of oncological mortality rates for BSSR, which were made on the basis of the collective dose for European USSR (75 million population), calculated by Soviet experts and submitted to the IAEA [International Atomic Energy Agency] [3], are apparently underestimated to 1/2-1/3 [the actual values], since they were calculated on the assumption of uniform radiation exposure of the entire population, whereas the population of BSSR was exposed to a considerably higher dose of radiation (if only because there are about

7000 km² contaminated territory in Belorussia, as compared to 1000 km² in the Ukraine and 2000 km² in RSFSR).

There are data to the effect that radiation-induced cases of leukemia constitute one-fifth of all postradiation tumors [2]. According to the data of the UN Scientific Committee on the Effects of Atomic Radiation [SCEAR], with an absorbed radiation dose of 10 mGy (1 rad), the risk of leukemia constitutes 20/100,000 people (quoted form [2]).

On the basis of these data, our estimates warrant the belief that the number of leukemia-caused deaths in BSSR may range from 12,280 to 18,420 cases over a 50-year period (250-350 cases per year). The figures will be even higher if we proceed from the estimates of J. Scheer [6] for FRG and our estimates for Belorussia based on them, 16,667-33,334 cases (370-670 per year).

In the article, "Ecological Distinctions and Biomedical Sequelae of the Accident at the Chernobyl AES," [5] by a large team of authors (25 scientists) headed by L. A. Ilyin, based on vast factual material, it was shown rather convincingly that additional deaths due to malignant neoplasms induced by radiation can reach only 0.5-0.7 percent of the spontaneous level. We should like to believe this, but the new data that are constantly being obtained on levels of radionuclide contamination of populated centers and the illegal ban of the USSR Ministry of Health on diagnosing radiation-induced lesions in individuals stricken as a result of the Chernobyl accident prompts cautiousness, to put it mildly. One could question the estimates of authors concerning extent of radiation exposure of the public in the early weeks after the accident and doubt the forecasts about future morbidity and mortality from intake of radionuclides with foodstuffs.

R. Clark, secretary of the Scientific Committee for Radiation Safety of Great Britain, announced in

November 1986, at a conference dealing with biological aspects of ionizing radiation (quoted from R. R. Jones) that no single epidemiological study would be able to demonstrate the direct effects of the Chernobyl accident due to the small number of additional cancer deaths (1000 in EEC [European economic community] countries in the next 50 years) against the background of the usual projection (30 million). However, as noted by R. R. Jones [8], one can expect 8000, rather than 1000, additional deaths in EEC countries in the next 50 years, although it will be just as difficult to detect them as 1000 cases. At the same time, on the basis of estimates of the risk of thyroid cancer (2500 additional cases against the background of the projected spontaneous 30,000-40,000 cases), he believes that it is possible to detect this increment in an epidemiological study. All of the foregoing applies to EEC countries.

The situation that has developed in stricken parts of the Soviet Union is considerably more complex, while the forecast is, of course, much more serious than for EEC nations.

The forecast of long-term sequelae of the accident at the Chernobyl AES for FRG, made by J. Scheer [6], is too gloomy, whereas the expected mortality due to oncological diseases (also for FRG) cited by R. R. Jones [8] (3000 cases) most likely reflects the actual situation.

For the sake of comparison we estimated possible long-term sequelae of the Chernobyl accident on the basis of collective radiation doses to the inhabitants of Belorussia cited by L. A. Ilyin et al. [5] and the above-described recommendations of international committees and commissions (NKEZ and ICRP) for radiation damage (Table 1). As can be seen from this table, even if we proceed from 501 cases of death due to oncological diseases induced by radiation and the correction factor for extremely low dose rate (about 0.01 rem/day), which is generally considered to be 5 (L. A. Ilyin et al.), we obtain figures that differ appreciably from those cited in "Ecological Distinctions and Biomedical Sequelae of the Accident at the Chernobyl AES."

Table 1. Possible long-term sequelae of the Chernobyl accident in the population of Belorussia

Regions	Population, millions	Collective dose, million man/rem	Additional deaths		Spontaneous deaths, thous.		Excess over spontaneous level, percent	
			leukemia	other malignant diseases	leukemia	other malignant diseases	leukemia	other malignant diseases
Southeastern	2.96	8.5	24	284	13	420	0.236	0.076
Northwestern	7.05	1.9	5	63	31	1001	0.022	0.007
Totals*	10.01	10.4	29	347	43	1422	0.085	0.027
Southeastern	2.96	8.5	340	8517	13	420	2.615	2.028
Northwestern	7.05	1.9	76	190	31	1001	0.245	0.019
Totals**	10.01	10.4	416	8707	43	1422	0.967	0.612

Footnotes: *Data taken from Table 14 of L. I. Ilyin et al. [5]. **Estimate of oncological diseases according to recommendations of Committee on Biological Effectiveness of Ionizing Radiation (501 cases per 10,000 man-Sv; 20 cases of leukemia per 100,000 man-rad, with correction factor 5 for very low radiation dosage).

The article by V. I. Ternov et al. [7], in which analysis is made of the effects of ^{137}Cs of global origin on the Belorussian people, merits attention.

In 1963, residents of Belorussia consumed 447 pCi/day ^{137}Cs with food, as a result of which an internal radiation dose of 8.1 mrad-man of internal radiation was formed (the dosage from the natural gamma-ray background is 110 mrad-man/year). The probability of oncological disease in 1963 as a result of internal exposure to radiation from incorporated ^{137}Cs could constitute 8 cases per 10^6 people, which corresponds to 0.4 percent rise in spontaneous oncological morbidity [7].

After the accident at the Chernobyl AES, foodstuffs began to contain significant amounts of ^{137}Cs which would apparently be expressed in nCi or even mCi, rather than pCi (i.e., 1000 or 1,000,000 times more), and for this reason one should expect a considerably greater increase in incidence of malignant neoplasms.

The data we have cited about sequelae of the Chernobyl accident with respect to health of people in stricken regions are contradictory, and only time will enable researchers to determine the validity of their conclusions and forecasts.

Nevertheless, the forecast of additional oncological disease submitted here provides sufficient grounds for raising the question of immediate construction of a hematological clinic with modern equipment, since there is no specialized modern, well-equipped hematological clinic in BSSR, either for children or adults. This is one of the causes of differences in indicators of 5-year survival rate in remission among acute leukemia patients: 2-3 percent for adults and 6-10 percent for children, whereas abroad the figures are 30 and 50 percent, respectively [4]. These data render the forecast of additional deaths due to leukemia even more gloomy for residents of BSSR: while the number of radiation-induced leukemia cases constitutes one-fifth of all neoplasms according to the data cited by V. Ya. Golikov et al. [2] and according to data cited by I. Ya. Vasilenko et al. [1] one-third to one-half of radiation-induced oncological diseases with fatal outcome, considering the adverse indicators of survival of leukemia patients cited by L. G. Kovalev et al. [4], the conversion of data on additional incidence of radiation-induced leukemia in BSSR should constitute one-third, rather than one-fifth. Failure to adhere to the set of aseptic and antiseptic measures for prevention of infections alone, which is impossible to provide even in the best modern therapeutic hospitals, virtually nullifies in many instances the enormous expense of treatment for patients with acute leukemia, which prolongs the lives of some of them by only 3-6 months. This is why construction of a modern hematological center, including a hospital for adults (at least 300 beds) and children (at least 150-200 beds) should become a priority task for today. It is inexpedient to separate these two hospitals, since clinical hematology is one of the clinical disciplines for which continuity and uniformity is absolutely inherent in the treatment of

both children and adults (suffering from leukemia, hemophilia, hemorrhagic vasculitis, etc.).

The same center, when well-equipped and making broad use of computerization, would be the methodological-educational and scientific base for the department of hematology and blood transfusions of the Institute for Advanced Training of Physicians and hematology course at the Medical Institute. The closeness of the Belorussian Scientific Research Institute of Hematology and Blood Transfusion and the Republic Blood Transfusion Center to the hematological center would permit sophisticated examination of patients in order to make the correct diagnosis, prompt treatment with blood preparations and use of plasmapheresis, lymphadsorption and hemadsorption, and bone marrow transplants.

The acute need for opening such a clinic is related not only to the fact that radiation-induced leukemia is one of the most frequent diseases induced by ionizing radiation, but also that the latency period of leukemia is several times shorter than that of other oncological diseases.

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UDC 612.014.482:616-073.786(476)

Radiometric Monitoring of Radiation Exposure of Belorussian Population

907C0862N Minsk ZDRAVOOKHRANENIYE BELORUSSII in Russian No 6, Jun 90 (manuscript received 14 Feb 90) pp 60-61

[Article by V. F. Minenko, and A. V. Ulanovskiy, Minsk]

[Text] As a result of radioactive fallout during the accident at the Chernobyl AES [nuclear power plant], at the present time there are 2257 populated centers in BSSR [2] with a population of more than 726,000 that are in a zone with 1 Ci/km² or more ^{137}Cs contamination of soil. The life of people in this area constantly involves the risk of intake of radioactive substances via respiratory organs, the skin and, mainly, with food. In areas with low density of radioactive contamination, the level of migration of radioactive substances from soil to plants and in the food chains to man is tens of times higher than in soil with much higher contamination of soil. As a result, one may encounter both individuals and populated centers exposed to a mean annual radiation dose in excess of 0.5 rem, which is stipulated in the radiation safety standards [3], over the entire territory where density of ^{137}Cs contamination is greater than 1 Ci/km². According to our estimates, of the 700 populated centers with expected exposure to a mean annual dose of more than 0.5 rem in 1989, more than 300 populated centers are in the zone of 15 Ci/km². In such a situation, continuous radiometric monitoring of food and direct in vivo radiometry of the human body continue to be necessary measures for early prevention of incorporation of radioactive substances and protection of people against internal radiation.

The main instrumentation for direct readings of human radioactivity in the BSSR is the human radiation counter (HRC) with shadow shielding. At the present time there are 20 domestic and foreign HRC units in this republic. They are located permanently in central rayon hospitals of the most contaminated rayons of Gomel (9), Mogilev (6), Brest (2) oblasts, and 3 are in the city of Minsk, at the Belorussian Scientific Research Institute of Radiation Medicine. This distribution of the units makes it possible to effect permanent monitoring of the population annually in the zone with the worst radiation conditions inhabited by more than 100,000 people.

In 1988, 44,700 people were screened on the HRC units, and about 69,000 were screened in 9 months of 1989. In addition to the units installed in rayons where there were none, high-speed monitoring of radioactive substances is implemented by means of the SRP-68-01 research radiometer using a technique developed in 1987 [1]. Using SRP-metry, more than 70,000 people were screened in 1988 and about 13,000 in 1989. The high output and simplicity of using SRP-metry makes it possible to screen a large number of people at the places of their residence; however, its low sensitivity and high margin of error of readings limits its use only to assessment of elevated radionuclide content (more than 1 μCi per person).

In order to organize a system of really mass-scale monitoring of internal radiation in the people of Belorussia, it is imperative, first of all, to establish groups of 2-4 portable HRC units in areas with radioactive contamination, with clearly prepared schedules and itineraries over contaminated regions; a specialized republic service center must be established to service all HRC units with a sufficient replacement supply of spare parts; the process of taking readings and obtaining results on all HRC units must be automated; it is imperative to adopt SRP-metry in all contaminated regions, to be carried out by the personnel and resources of rayon sanitary and epidemiological stations for immediate detection of individuals with elevated internal radionuclide levels and screening of those to be rechecked on human radiation counters.

When combined with the existing system, the new structure will make it possible to cover at least 500,000 people with radiometric monitoring of internal radiation.

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UDC 612.014.482:614.7(476)

Gamma Background in Belorussian SSR

907C08620 Minsk ZDRAVOOKHRANENIYE
BELOUSSII in Russian No 6, Jun 90 (manuscript
received 18 Oct 89) pp 61-62

[Article by V. I. Ternov, and A. G. Kondratyev, Belorussian Institute for Advanced Training of Physicians]

[Text] The natural gamma background is an inalienable element of the biosphere that is actively involved in the evolutionary process. Its quantitative evaluation is still an important task for radiation medicine, since it permits having a sort of reference point, from which one should start when analyzing the intensity of effects on man of other sources of radiation.

To date, no data have been published on the natural gamma background in Belorussian SSR, and this was the reason for our investigation.

During 1981-1982, along with specialists from the sanitary and epidemiological service, we measured the gamma background in the cities of Minsk, Vitebsk, Borisov and Soligorsk, as well as in rural areas of Minskiy Rayon. In all, we took 3540 readings, including 655 in cities and villages and 28,885 in residential

buildings. The gamma background was measured with the SRP-68-01 instrument [research dosimeter] in an open area, in populated centers (out of doors) and in residential buildings built of different construction materials: wood, bricks, reinforced concrete. At each point we took 5 readings at a height of 2 m from the measured surface. We took into consideration the equivalence of gamma background vertically in a building [1], measurements in multistory buildings were taken on the second-floor landing.

Calculation of exposure dose rate from gamma radiation for urban residents was carried out using the following formula: $P = 0.2 P_{od} + P_{bld}$ $\mu R/h$, where 0.2 and 0.8 are coefficients corresponding to time spent by residents out of doors [od] and in buildings [bld] [2].

These coefficients were considered to be 0.4 and 0.6, respectively, for rural residents. We subtracted from the result the dose rates attributable to stratospheric fallout of radioactive products which, according to the data in [3], constituted 0.77 mrad/year for urban residents and 2.15 for rural residents in 1975.

The results are listed in the table. According to these data, the gamma background in different cities fluctuates over a narrow range, constituting 10.0/12.1 $\mu R/h$ (arithmetic mean = $10.6 \pm 0.8 \mu R/h$).

Values for gamma background (R/h)

Observed zones	Gamma background of territory	Wood buildings	Brick buildings	Reinforced concrete buildings	Mean dose rate
Minsk	10.4+/-0.9	11.3+/-1.7	16.6+/-1.3	15.3+/-1.4	13.9
	(28)	(87)	(200)	(83)	
Vitebsk	12.1+/-1.3	12.0+/-0.8	19.0+/-1.6	21.0+/-1.5	16.2
	(27)	(13)	(36)	(23)	
Soligorsk	10.0+/-1.0	—	17.5+/-1.7	16.5+/-2.6	15.6
	(20)		(13)	(15)	
Borisov	10.0+/-0.9	11.0+/-1.3	19.0+/-3.0	18.0+/-2.1	14.8
	(17)	(14)	(18)	(10)	
Means for cities	10.6+/-0.8	11.4+/-0.8	17.8+/-2.3	17.7+/-2.4	15.1
Rural area	9.0+/-0.8	10.2+/-1.1	15.0+/-1.5	—	13.1

Note: Number of points where readings were taken is given in parentheses.

In rural areas the gamma background constituted $9.0 \pm 0.8 \mu R/h$.

Measurement of gamma background in buildings made of different construction materials revealed that the lowest radiation level was observed in wood structures. Gamma background in brick and reinforced concrete buildings in cities did not differ appreciably, constituting a mean of 17.8 ± 2.3 and $17.7 \pm 2.4 \mu R/h$, respectively.

Weighted mean gamma radiation dose rate was 15.1 $\mu R/h$ in urban areas and 13.1 $\mu R/h$ in rural areas.

Cumulative annual doses of radiation from the gamma background constituted 131.8 mrad for urban residents and 112.6 mrad for rural inhabitants.

On the basis of these studies, it can be maintained that at the time of the measurements the territory of Belorussia was referable to regions with typical level of natural gamma background, which is inherent in most parts of the USSR and the world [4, 5].

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UDC 618.36-002-022.7:578.891]-053.31-084

Perinatal Infection of Children with Hepatitis B Virus and Specific Prophylaxis

907C0086C Moscow *VESTNIK AKADEMII MEDITSINSKIKH NAUK in Russian* No 7, Jul 90 (manuscript received 1 Nov 89) pp 29-32

[Article by I. V. Sakhgildin, N. A. Farber, S. N. Kuzin, S. G. Cheshik, Zh. A. Drobenyuk, M. I. Mikhaylov, P. A. Khukhlovich, M. A. Gorbunov, V. N. Ikoyev, T. V. Golosova, A. N. Margolina, M. I. Tsvayner, P. I. Yarovoy, K. A. Khalitova and A. Ya. Buriyev, Institute of Virology imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences, Moscow]

[Abstract] Studies were conducted on the incidence of perinatal hepatitis B in neonates in relation to maternal HBsAg carrier state in Moscow (18,652 women), Bendery (Moldavia) (2539) and Karshi and Fergan (Uzbekistan) (6142). The percentage of HBsAg positive women in Moscow, Uzbekistan and Moldavia was 1.1, 6.9 and 5.4 percent, respectively. The corresponding HBeAg positive rate was 5.2, 13.9 and 16.3 percent. Serologic monitoring of the newborn showed that 26.1 percent were HBsAg positive in Moscow, and 40 percent in Uzbekistan and Moldavia. However, whereas the HBsAg positive status of the Moscow newborn was transient, in 16.0 percent of the Uzbek children and 13.3 percent of the Moldavian children the HBsAg carrier state persisted with development of primary chronic hepatitis B. Experience has also shown that use of anti-hepatitis B vaccines and specific immunoglobulin preparations for prophylaxis in neonates appears to be warranted in areas with a high incidence of HBsAg and HBeAg positive gravid women. Such practice is not recommended in areas with a low incidence of HBsAg and HBeAg positive mothers, the majority of whom are

also anti-HBe positive, since the probability of a persistent HBsAg positive status in neonates is negligible. Tables 1; references 18: 7 Russian, 11 Western.

UDC 618.33-007-02:613.63]-07

Occupational Risk Factors in Perinatal Pathology

907C0086B Moscow *VESTNIK AKADEMII MEDITSINSKIKH NAUK in Russian* No 7, Jul 90 (manuscript received 4 Nov 89) pp 26-29

[Article by I. F. Izmerov and Z. A. Volkova, Scientific Research Institute of Labor Hygiene and Occupational Diseases, USSR Academy of Medical Sciences, Moscow]

[Abstract] A brief review is provided of occupational risk factors as reflected in perinatal pathology, leading to fetal distress, toxemia of pregnancy, and neonatal morbidity. Nevertheless, improvements in working conditions and control of noxious substances at worksites have had telling effects. To date, such measures have resulted in a 3.5-fold reduction in spontaneous abortions, a 1.5-fold decrease in complications of pregnancy, and a 4.5-fold decrease in severe toxemias of pregnancy. The data indicate that rigorous implementation and enforcement of health regulations in the occupational setting, in conjunction with further improvements in clinical care and preventive practices, may be expected to further improve maternal and child health and alleviate the adverse effects of industrial development. Tables 3; references 8 (Russian).

UDC 618.3-02:614.7]-7

Occupational Factors and Pregnancy

907C0086A Moscow *VESTNIK AKADEMII MEDITSINSKIKH NAUK in Russian* No 7, Jul 90 (manuscript received 10 Oct 89) pp 23-25

[Article by E. K. Aylamazyan, Institute of Obstetrics and Gynecology imeni D. O. Ott, USSR Academy of Medical Sciences, Leningrad]

[Abstract] An analysis was conducted on the impact of occupational health factors on the course and outcome of pregnancy in the case of 631 women employed in polymer processing, rubber and footwear plants (Group I), 314 in the electronics industry (Group II), and 260 who occupation did not entail hazardous exposure (Group III). The key health hazards in the first two groups were exposure to benzene, chloroprene, ethyl acetate, methyl methacrylate, dimethylformamide and hydrogen fluoride, as well as hypokinesia and stress. The clinical statistics revealed that the incidence of fetal loss in the first two groups were on the order of 24.7 to 26.2 percent, and that premature termination of pregnancy was 8.9- and 12.4-fold greater for these two respective groups than for the control subjects. In addition, late toxemia of pregnancy was a complication in 27.8 percent of group I workers and 32.4 percent of group II workers.

Pathologic studies on the placentas demonstrated an elevated incidence of immune-complex deposits encompassing the three major Ig classes in Groups I and II in comparison with Group III. Neonates born to women in groups I and II were 2- to 3-times as likely to have low Apgar scores as in the case of Group III women, and 42 percent were threatened with fetal asphyxia (vs. 18 percent for Group III.) Pathophysiologic considerations led to the conclusion that during the first 3 years of employment the Group I and II women underwent a phase of acute physiological deadadaptation, followed by a phase of chronic subcompensation. The latter was followed by a phase of chronic decompensation and depletion of physiological reserves resulting in essentially irreversible damage to their reproductive potential.

UDC 616.1-036.88(575.1)

Mortality Rate of Chief Cardiovascular Diseases in Uzbek SSR

917C0062B *Tashkent MEDITSINSKIY ZHURNAL UZBEKISTANA in Russian No 7, Jul 90 (manuscript received 11 Oct 89) pp 32-34*

[Article by R. T. Sultanov, L. V. Mironova, D. A. Khamidova, R. Sh. Mamutov, and N. L. Mirzayev, Public Health Ministry, Uzbek SSR, Cardiology Scientific Research Institute, Uzbek SSR Ministry of Health]

[Abstract] The data for circulatory system disease mortality spanning 1975-1985 in Uzbekistan were analyzed by sex, age, and locality to reveal regional aspects of mortality and assess the effects of sociodemographic and medical and organization factors. The data revealed a 12 percent increase in circulatory system disease mortality from 1975-1980, at which time mortality stabilized. It was also shown that one-third of all deaths in Uzbekistan were due to circulatory system diseases. The wide fluctuations in mortality due to circulatory system diseases from urban (Tashkent, 51.5 percent) to rural areas (Surkhandarin, 18.7 percent) were ascribed to regional aspects as well as abilities to correctly determine the cause of death. It was shown that the incidence of ischemic heart disease increased 2.7 times (from 3.5 to 9.3 percent) for those aged 50-59 years. The main causes of death among the working population were shown to be myocardial infarct and hypertension, while it was ischemic heart disease and vascular blockages in the brain among the elderly. Perhaps most alarming of all the data was the distinct increase in circulatory system diseases among younger people.

UDC 616.7-002(575.1)

Tuberculosis of Bones and Joints Incidence in Rural Uzbek SSR

917C0062A *Tashkent MEDITSINSKIY ZHURNAL UZBEKISTANA in Russian No 7, Jul 90 pp 28-29*

[Article by P. Kh. Nazirov, Scientific Research Institute of Phthisiology and Pulmonology imeni Sh. A. Alimov, Uzbek SSR Ministry of Health]

[Abstract] During the 1975-1986 the incidence of tuberculosis of the bones and joints (TBJ) in rural areas has decreased by only 35.5 percent, as opposed to a 50 percent reduction for urban areas, with the TBJ incidence currently two-and-one-half times higher in rural areas than in the city. Uzbekistan had previously been thought to have a low TBJ infection rate among cattle, who are the chief carriers of the disease, but recent studies demonstrated that more than 11,000 head were infected, of which 80 percent were slaughtered. The epidemic TBJ situation is blamed on a number of factors, including: 1. a low standard of living—lack of plumbing and sewage disposal means, use of unpurified water from reservoirs, and poor nutrition; 2. poorly trained veterinary personnel conduct the examination; and 3. modern, effective diagnostic techniques are not being used and result in late diagnosis and increasing numbers of people with acute forms of the disease. Recommendations for combatting TBJ include early detection, the development and use of new, effective diagnostic and treatment techniques for TBJ, and semi-annual examination of farms with a history of TBJ problems.

UDC 371.7(575.1-25)

Health Status of Public School Students in Tashkent

917C0043A *Moscow GIGIYENA I SANITARIYA in Russian No 6, Jun 90 (manuscript received 17 Mar 89) pp 29-30 hepatitis. The patients were divided into two groups treated*

[Abstract] The health status of 3,285 students aged 6-11 years in five public schools in Tashkent was investigated using health records maintained for 5 years. The overall morbidity was 7,338.8 cases per thousand. Morbidity is highest at age six, and then steadily decreases, with a second peak occurring at age 11. The high incidence of respiratory organ complaints, the most frequent disorder (69.7 percent), was attributed to pollution and great daily fluctuations in temperature. In second place were infectious and parasitic diseases (12.5 percent) such as chicken pox, parotitis, infectious hepatitis, and helminthoses, with morbidities of 189.4 and 106.5 per thousand for the latter two. Nervous system and sensory organ disorders occupied third place. The results demonstrated that boys were more susceptible to illnesses than girls. The surge in morbidity among eleven-year-olds was attributed to the prevalence of chronic disorders. Based on these data, the students were placed in the following health groups: I - 29.3 percent; II - 40.7 percent; III - 29 percent; IV - 1 percent. Tables 2.

Fourth Main Directorate of Uzbek Ministry of Health Abolished

917C0047A *Tashkent SELSKAYA PRAVDA in Russian 15 Sep 90 p 3*

[Unattributed article]

[Abstract] In accordance with the resolutions of the USSR Supreme Soviet and the Supreme Soviet of the Uzbek SSR, and considering the many requests by workers, and in order to implement the principles of social justice, the Council of Ministers of the Uzbek SSR has announced that the fourth main directorate of the Uzbek Ministry of Health has been abolished effective 1 October 1990. A liquidation commission has been set up for this purpose. The decree is printed, and a brief explanation indicates that the abolition is intended to further strengthen the material basis of public

health, particularly strengthening preventive pediatric medicine in large families. One of the hospitals made available by the abolition will be used to set up a "mother and child" center for effective treatment of mothers with children. Patients from all regions of the republic will be sent to this center. Each year, over 2000 children and parents will receive rehabilitation treatment at "Uzbekistan" Sanatorium in Yalta. 60 percent of these visits have been allocated for the karakalpak ASSR. Preference will be given to war and labor veterans.

UDC 619:661.879:591.444

**Thyroid Effects in Ruminants of Radionuclides
Emitted in Chernobyl Accident**

907C0079C Moscow *VETERINARIYA in Russian* No
7, Jul 90 pp 60-63

[Article by V. A. Budarkov, N. I. Arkhipov, A. S. Zenkin, R.
M. Yunosova and Yu. A. Yastrebkov, All-Union Scientific
Research Institute of Veterinary Virology and Microbiology]

[Abstract] Histopathological and clinical observations
were conducted on 400 heads of cattle and sheep in

Gomel Oblast to assess the thyroid effects of iodine
radionuclides emitted in the Chernobyl accident. The
studies were conducted over a 3 year period spanning
1986-1989 and showed that the average radiation dose
delivered to the thyroid gland ranged from 1 to 4 krads,
although in some animals the dose reached 10 k rad.
Thyroid pathology became evident 5 to 8 months after
the accident and its manifestations were evident
throughout the 3 year period of observation. In general,
the predominant thyroid pathology consisted of atrophy
with some cases of hyperthyroidism and attendant met-
abolic sequelae, a two-fold reduction in fertility and
congenital anomalies in newborn. Figures 4.

UDC 619:576.8.097.3:615.371/.372:576.858.13

Reactogenic and Immunogenic Properties of Sheep Pox Vaccine*907C0079B Moscow VETERINARIYA in Russian No 7, Jul 90 pp 28-30*

[Article by V. N. Ivanyushchenkov, V. G. Kekukh and O. A. Koreba]

[Abstract] Reactogenicity and immunogenicity trials were conducted with a dry NISKhI sheep pox vaccine on sheep ranging in age from 1 month to 6 years. The results demonstrated that the vaccine was areactogenic on subcutaneous injections in fine-fleeced Kazakh and karakul breeds, eliciting neutralizing antibodies within 4 to 5 days. The immune response was observed to persist for at least a year. Tables 3; references 17: 5 Russian, 12 Western.

Various Methods of Vaccinating Poultry Against Newcastle Disease*917C0026A Moscow VETERINARIYA in Russian No 6, Jun 90 pp 32-34*

[Article by E. G. Khorguani, Transcaucasus Division of VNIIVS [as published]]

[Abstract] The effectiveness of various methods of vaccinating poultry against Newcastle disease, one of the most serious illnesses that affects poultry, was investigated by using white leghorn, cross 266 chicks. Peroral, intranasal, moist aerosol, or dust aerosol immunization with a dry La-Sota strain of the vaccine was performed at 5-6 days and 35-40 days of age, with each method of immunization assessed for immunologic effectiveness, actual vaccine consumption, labor cost (man hours), and other economic indices. Specific antibodies were shown to develop 2-3 days earlier in chickens vaccinated with a dust aerosol, but by days 14-16 antihemagglutinin titers in the blood of all the chickens were approximately equivalent, except for animals immunized perorally. These results, in addition to data on vaccine consumption and labor cost, demonstrate that dust aerosol vaccination of poultry against Newcastle disease is the most effective both immunologically and economically. Tables 2; references 8 (Russian).

UDC 577.152.321:577.113.5

Comparison of Primary Structure of 26 S RNA in Eastern Equine Encephalomyelitis Virus Variants

907C0844b Moscow DOKLADY AKADEMII NAUK
SSSR in Russian Vol 313, No 1, Jul 90 (manuscript
received 28 Dec 89) pp 216-219

[Article by V. Ye. Volchkov, V. A. Volchkova, I. V. Frolov, A. A. Kolykhalov, S. V. Netesov, and L. S. Sandakhchiyev Associate Member, USSR Academy of Sciences; All-Union Scientific Research Institute of Molecular Biology, Koltsovo Settlement, Novosibirsk Oblast]

[Abstract] A set of recombinant plasmids were obtained from the synthesized DNA of the Eastern Equine

Encephalitis virus, which contained the entire nucleotide sequence of the viral 26 S RNA. Screening of insertions into these plasmids led to a determination of the primary structure of the viral 26 S RNA, which was compared to the primary structure of the American variant. A high degree of homology was observed. In the 3'-noncoding area there were only 10 substitutions and 3 single-nucleotide deletions. One substitution was found in the 5' noncoding region and none in the E3 gene. Two groups of differences were found in the structural protein regions, one containing several substitutions and the other involving reciprocal inversions. Some of the first group differences are in the possible antigenic determinant. Differences were observed in the 380-389 region of the E2 protein, the hydrophobic "anchor", and in the 319-350 area of the E1 protein. Figures 1; references 10; Western.

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